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TABLE OF CONTENTS

HEADER 1
ABSTRACT 1
PLAIN LANGUAGE SUMMARY 2
BACKGROUND 2
OBJECTIVES 3
METHODS 4
RESULTS 6
Figure 1. 10
DISCUSSION 14
AUTHORS' CONCLUSIONS 15
ACKNOWLEDGEMENTS 16
REFERENCES 16
CHARACTERISTICS OF STUDIES 21
DATA AND ANALYSES 42
Analysis 1.1. Comparison 1 Mirror therapy versus all other interventions: primary and secondary outcomes, Outcome 1 Motor function at the end of intervention phase. 44
Analysis 1.2. Comparison 1 Mirror therapy versus all other interventions: primary and secondary outcomes, Outcome 2 Activities of daily living at the end of intervention phase. 46
Analysis 1.3. Comparison 1 Mirror therapy versus all other interventions: primary and secondary outcomes, Outcome 3 Pain at the end of intervention phase. 47
Analysis 1.4. Comparison 1 Mirror therapy versus all other interventions: primary and secondary outcomes, Outcome 4 Visuospatial neglect at the end of intervention. 47
Analysis 1.5. Comparison 1 Mirror therapy versus all other interventions: primary and secondary outcomes, Outcome 5 Motor function at follow-up after 6 months. 48
Analysis 2.1. Comparison 2 Subgroup analysis: upper versus lower extremity, Outcome 1 Motor function at the end of intervention. 49
Analysis 3.1. Comparison 3 Subgroup analysis: sham intervention (covered mirror) versus other intervention (unrestricted view), Outcome 1 Motor function at the end of intervention phase. 50
Analysis 4.1. Comparison 4 Sensitivity analysis by trial methodology, Outcome 1 Motor function at the end of intervention. 51
Analysis 5.1. Comparison 5 Post-hoc sensitivity analysis removing studies that only included patients with CRPS after stroke, Outcome 1 Motor function at the end of intervention. 54
Analysis 5.2. Comparison 5 Post-hoc sensitivity analysis removing studies that only included patients with CRPS after stroke, Outcome 2 Pain at the end of intervention phase. 55
Analysis 5.3. Comparison 5 Post-hoc sensitivity analysis removing studies that only included patients with CRPS after stroke, Outcome 3 Motor function at follow-up after 6 months. 56
ADDITIONAL TABLES 56
APPENDICES 63
CONTRIBUTIONS OF AUTHORS 65
DECLARATIONS OF INTEREST 65
SOURCES OF SUPPORT 65
DIFFERENCES BETWEEN PROTOCOL AND REVIEW 66
INDEX TERMS 66

[Intervention Review]

Mirror therapy for improving motor function after stroke

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ABSTRACT

Background

Mirror therapy is used to improve motor function after stroke. During mirror therapy, a mirror is placed in the patient's midsagittal plane, thus reflecting movements of the non-paretic side as if it were the affected side.

Objectives

To summarise the effectiveness of mirror therapy for improving motor function, activities of daily living, pain and visuospatial neglect in patients after stroke.

Search methods

We searched the Cochrane Stroke Group's Trials Register (June 2011), the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2011, Issue 2), MEDLINE (1950 to June 2011), EMBASE (1980 to June 2011), CINAHL (1982 to June 2011), AMED (1985 to June 2011), PsycINFO (1806 to June 2011) and PEDro (June 2011). We also handsearched relevant conference proceedings, trials and research registers, checked reference lists and contacted trialists, researchers and experts in our field of study.

Selection criteria

We included randomised controlled trials (RCTs) and randomised cross-over trials comparing mirror therapy with any control intervention for patients after stroke.

Data collection and analysis

Two review authors independently selected trials based on the inclusion criteria, documented the methodological quality of studies and extracted data. We analysed the results as standardised mean differences (SMDs) for continuous variables.

Main results

We included 14 studies with a total of 567 participants that compared mirror therapy with other interventions. When compared with all other interventions, mirror therapy may have a significant effect on motor function (post-intervention data: SMD 0.61; 95% confidence interval (CI) 0.22 to 1.0; P = 0.002; change scores: SMD 1.04; 95% CI 0.57 to 1.51; P < 0.0001). However, effects on motor function are influenced by the type of control intervention. Additionally, mirror therapy may improve activities of daily living (SMD 0.33; 95% CI 0.05 to 0.60; P = 0.02). We found a significant positive effect on pain (SMD -1.10; 95% CI -2.10 to -0.09; P = 0.03) which is influenced by patient population. We found limited evidence for improving visuospatial neglect (SMD 1.22; 95% CI 0.24 to 2.19; P = 0.01). The effects on motor function were stable at follow-up assessment after six months.

Authors' conclusions

The results indicate evidence for the effectiveness of mirror therapy for improving upper extremity motor function, activities of daily living and pain, at least as an adjunct to normal rehabilitation for patients after stroke. Limitations are due to small sample sizes of most included studies, control interventions that are not used routinely in stroke rehabilitation and some methodological limitations of the studies.

PLAIN LANGUAGE SUMMARY

Mirror therapy for improving motor function after stroke

Paralysis of the arm or leg is common after stroke and frequently causes problems with activities of daily living such as walking, dressing or eating. Mirror therapy is a rehabilitation therapy in which a mirror is placed between the arms or legs so that the image of the non-affected limb gives the illusion of normal movement in the affected limb. We found 14 relevant studies involving 567 participants. At the end of treatment, mirror therapy improved movement of the affected limb and the ability to carry out daily activities. Mirror therapy reduced pain after stroke, but only in patients with a complex regional pain syndrome. The beneficial effects on movement were maintained for six months, but not in all study groups. No adverse side effects were reported. Further research is needed with larger studies in natural clinical settings, and with a comparison of mirror therapy with more routine treatments.

BACKGROUND

Description of the condition

Cerebrovascular diseases, taken together with ischaemic heart diseases, are the leading causes of death worldwide (WHO 2008). Each year approximately nine million people suffer a first-ever stroke. Stroke is one of the leading causes of long-term disability, particularly in high- and middle-income countries (WHO 2008). Immediately after stroke onset, approximately 80% of survivors have an upper or lower limb motor impairment (Barker 1997; Jorgensen 1995; Nakayama 1994). Full upper limb function is achieved by nearly 80% of patients with mild paresis, but only by 20% of patients with severe paresis of the upper limb (Nakayama 1994). Of those patients with an initial plegic upper limb, only half regain some motor function in the paretic upper limb six months later (Kwakkel 2003). Two-thirds of patients with lower limb impairment are not able to walk independently soon after their stroke, and after rehabilitation only half have independent walking function (Jorgensen 1995). The initial severity of upper and lower extremity paresis is one of the most important predictors of long-term functional recovery after stroke (Hendricks 2002; Jorgensen 1995; Nakayama 1994), but variability is high, possibly influenced by therapeutic interventions.

Up to 50% of patients experience pain of the upper extremity during the first 12 months post-stroke, especially shoulder pain and complex regional pain syndrome-type I (CRPS-type I) (Jönsson 2006; Kocabas 2007; Lundström 2009; Sackley 2008). Pain after stroke may restrict activities of daily living and reduce quality of life (Jönsson 2006; Lindgren 2007).

Additionally, about 40% of patients with an acute right hemispheric and 20% of patients with a left hemispheric stroke presented with a unilateral neglect (Ringman 2004). After three months a unilateral neglect was present in about 15% of patients with a right and 5% of patients with a left hemispheric stroke

(Ringman 2004). Besides the spatial attention deficits, neglect is a negative factor for functional recovery (Farnè 2004; Katz 1999) and was found to be associated with a reduced health-related quality of life (Franceschini 2010).

Therefore, effective training strategies to promote motor recovery and activities of daily living, reduce pain or visuospatial neglect or both are needed to reduce the burden of stroke.

Description of the intervention

Evidence suggests that effective therapeutic interventions for regaining motor function should potentially focus on the practice of functional tasks (Van Peppen 2004). However, task-oriented training strategies, such as constraint-induced movement therapy (French 2007; Liepert 1998; Miltner 1999b; Taub 1993), require some degree of voluntary movement, therefore they are not applicable for patients with severe paresis after stroke. Novel training strategies for this patient population use electromechanical training devices (Mehrholz 2007; Mehrholz 2008), electrical muscle stimulation (Urton 2007) or repetitive passive or assistive movement stimulation (Feys 2004; Platz 2005).

As an alternative treatment approach, mirror therapy has been proposed as potentially beneficial (Ramachandran 1994). In contrast to other interventions, which employ somatosensory input to assist motor recovery (Feys 2004), mirror therapy is based on visual stimulation. During mirror therapy, a mirror is placed in the patient's midsagittal plane, thus reflecting the non-paretic side as if it were the affected side (Ramachandran 1995). By this setup, movements of the non-paretic limb create the illusion of normal movements of the paretic limb. One of the possible advantages of mirror therapy is the relatively easy administration and the possibility for self-administered home therapy for patients even with severe motor deficits. Mirror therapy was first described in Ramachandran 1995 and Ramachandran 1996 with the studies reporting the effects of mirror therapy on pain reduction in arm amputees. Furthermore, mirror therapy was claimed to alleviate hemiparesis after stroke (Ramachandran 1994). A pilot study confirmed the positive effects of mirror therapy on patients' movement ability in upper limb hemiparesis after stroke (Altschuler 1999).

Recently, some authors have described 'mirror-like' video or computer graphic setups, where a video or computer graphic image of the moving limb is presented as if it were the opposite one (Adamovich 2009; Dohle 2004; Dohle 2011; Eng 2007; Gaggioli 2004; Morganti 2003).

How the intervention might work

The concept of mirror therapy has been substantiated neurophysiologically. Evidence suggests that the same cortical motor areas that are active during observation of movements are involved in the performance of the observed actions (Grèzes 2001). Movement mirroring (i.e. the inversion of the visual feedback) leads to an additional activation of the hemisphere contralateral to the perceived limb laterality (Dohle 2004; Matthys 2009; Shinoura 2008). In normal people, the mirror illusion may increase cortico-muscular excitability (Fukumura 2007; Garry 2005). However, the precise mechanisms of the effect of mirror therapy in stroke patients remain speculative. As the visual image of the paretic limb is perceived similarly to the patients' own moving limb (Dohle 2004), the mirror illusion might prevent or reverse a learned non-use of the paretic limb (Liepert 1995). Also, by modulation of the cortico-muscular excitability, mirror therapy might directly stimulate motor recovery. Finally, mirror therapy was regarded as a variant of motor imagery training, which is based on repetitive imagination and mental rehearsal of motor tasks (Miltner 1998; Stevens 2003). Behavioural studies suggest that the experience of agency (the attribution of visual images of body parts as being controlled by oneself) relies on a tight temporal coupling of the visual feedback of active, but not passive movements (Longo 2009). Imaging studies suggest that mirrored computer graphic images are processed similarly to those of real movements (Adamovich 2009; Dohle 2011) as long as the temporal and spatial consistency with real movements does not fall below certain thresholds (Franck 2001). Thus, even technically generated images of a human moving limb can be integrated into the body scheme with the same sense of agency as during 'real' mirroring.

Regarding non-motor symptoms, mirror therapy was found to be effective in reducing pain in patients with CRPS-type I (McCabe 2003). The authors hypothesised that mirror therapy may normalise central sensory processing by providing a physiological image of the affected limb (McCabe 2003). Another study found significant effects of mirror therapy on reducing unilateral visuospatial neglect after stroke (Dohle 2009). The strong visual stimulus of watching self-induced movements in the neglected hemifield was postulated to be responsible for this effect.

Why it is important to do this review

Recently, randomised controlled trials (RCTs) have been conducted to evaluate the effectiveness of mirror therapy after stroke (Cacchio 2009a; Cacchio 2009b; Dohle 2009; Sütbeyaz 2007; Yavuzer 2008). These trials however, employed different outcome measures and only had small study samples. Ezendam 2009 and Rothgangel 2011 published systematic reviews on the effectiveness of mirror therapy in different conditions. However, their search strategies were limited and the authors did not provide pooled analyses.

OBJECTIVES

The main purpose of this review is to summarise the effectiveness of mirror therapy compared with no treatment, placebo or sham therapy, or other treatments for improving motor function after stroke. Further, this review aims to assess the effects of mirror therapy on activities of daily living, pain and visuospatial neglect.

METHODS

Criteria for considering studies for this review

Types of studies

We included RCTs and cross-over RCTs comparing mirror therapy (provided by a mirror or a simultaneous video or virtual setup) with any other therapy modality, no therapy or sham therapy. If we included cross-over RCTs, we only analysed the first period as a parallel group trial.

Types of participants

We included studies examining participants with a paresis of the upper or lower limb, or both, caused by stroke (all types, severity and stages of stroke) aged over 18 years. If we identified studies with mixed populations of patients with neurological conditions, we included those studies if separate data for stroke patients were available.

Types of interventions

Mirror therapy is defined as an intervention that uses a mirror to create a reflection of the non-paretic upper or lower limb, thus giving the patient visual feedback of normal movement of the paretic limb. Using this setup, different variations in the experimental protocol are possible (Dohle 2005; Nakaten 2009). We included studies that used direct mirroring of movement of any regimen and variation, i.e. including video or virtual reality settings. However, we only included those studies where the regimen and delivery of mirror therapy could be identified.
The control arm of the study could include a no treatment group, usual or standard practice, or any other control treatment (i.e. placebo or sham therapy). We excluded studies where the influence of mirror therapy could not be isolated due to the comparison of different mirror therapy regimens or delivery. We contacted trialists if regimen or delivery (or both) of mirror therapy or the control intervention was unclear.

Types of outcome measures

We evaluated outcome measures post-intervention (or change scores between pre- and post-intervention measures) and at follow-up after six months or longer.

Primary outcomes

The primary outcome was motor function. Due to the wide variety of outcome measures, we selected outcome measures to facilitate quantitative pooling. If more than one outcome measure was available we prioritised measures as follows.

- Upper limb and hand function:
  - Fugl-Meyer Assessment (Fugl-Meyer 1975) - upper limb or hand function or both;
  - Action Research Arm Test (Lyle 1981), Motor Assessment Scale (Carr 1985) - upper limb and hand function or both; and
  - Wolf Motor Function Test (Wolf 2001), Brunnstrom Stages of the Upper Extremity (Brunnstrom 1966), Motricity Index (Demeurisse 1980) - arm score.
- Lower limb function:
  - Fugl-Meyer Assessment - lower limb function (Fugl-Meyer 1975); and
  - Brunnstrom Stages of the Lower Extremity (Brunnstrom 1966).
- Global motor function:
  - Motor Assessment Scale (Carr 1985), Rivermead Motor Assessment Scale (Collen 1991).

However, if these scales were not available, we accepted other measurements that evaluate motor function.

Secondary outcomes

Secondary outcomes included measures of activities of daily living (e.g. Functional Independence Measure (Keith 1987), Barthel Index (Mahoney 1965)), pain (Visual Analogue Scale or Numeric Rating Scale) and visuospatial neglect. We also searched for reported adverse effects (e.g. swelling).

Search methods for identification of studies

See the 'Specialised register' section in the Cochrane Stroke Group module.

Electronic searches

We searched the Cochrane Stroke Group's Trials Register, which was last searched by the Managing Editor in June 2011, the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2011, Issue 2), MEDLINE (1950 to June 2011) (Appendix 1), EMBASE (1980 to June 2011) (Appendix 2), CINAHL (1982 to June 2011) (Appendix 3), AMED (1985 to June 2011), PsycINFO (1806 to June 2011) and the Physiotherapy Evidence Database (PEDro) (June 2011). We modified the MEDLINE and CINAHL search strategies for the other databases.

Searching other resources

In an effort to identify further published, unpublished and ongoing trials not available in the major databases we:

1. handsearched the following conference proceedings:
    - Deutsche Gesellschaft für Neurologie (2008, 2009);
    - Deutsche Gesellschaft für Neurorehabilitation (2000, 2001, 2003, 2005, 2007, 2009, 2010);
    - Deutsche Gesellschaft für Neurotraumatologie und klinische Neurorehabilitation (2005, 2007, 2009, 2010);
    - European Stroke Congress (2001 to 2009);
    - World Congress of Neurorehabilitation (1999, 2002, 2006, 2010);
    - World Congress of Physical Therapy (2003, 2007, 2011);
    - World Stroke Congress (2000, 2004, 2008, 2010);
2. screened reference lists of all relevant articles and books;
3. identified ongoing trials and research registers, including:
    - Current Controlled Trials (http://www.controlled-trials.com/) (searched June 2011);
    - ClinicalTrials.gov (http://clinicaltrials.gov/) (searched June 2011);
    - Stroke Trials Registry (http://www.strokecenter.org/trials/) (searched June 2011);
    - International Clinical Trials Registry Platform (ICTRP) (http://www.who.int/ictrp/en/) (searched June 2011);
4. contacted trialists, experts, researchers and commercial companies (Reflex Pain Management Ltd) in our field of study to obtain information of unpublished studies and studies not available in the electronic databases;
5. searched OpenSIGLE - System for Information on Grey Literature in Europe (http://www.opengrey.eu/) (searched June 2011); and
6. searched the REHABDATA database (http://www.naric.com/research/rehab/) (searched June 2011).

We did not impose any restrictions on language or publication status when deciding on including studies.

Data collection and analysis

Selection of studies

Two review authors (HT and CD) independently screened titles of the references identified from the electronic database searches and excluded obviously irrelevant references. We obtained abstracts or full texts or both of the remaining studies and used our inclusion criteria (types of studies, types of participants, types of interventions and outcome measures) to assess whether they were eligible for inclusion. We resolved disagreements by discussion. If the inclusion of a study was unclear due to missing information, we tried to contact the authors of the studies for further details.

Data extraction and management

Two review authors (HT and CD) independently extracted trial and outcome data of the included trials using a checklist. Because one author (CD) is principal investigator of an included trial, another author (JB) did the data extraction of this study. The checklists for data extraction contained:

- methods of randomisation;
- methods of concealment of allocation;
- blinding;
- use of an intention-to-treat (ITT) analysis (all participants initially randomised were included in the analysis as allocated to groups);
- adverse events;
- drop-outs for all reasons;
- imbalance of important prognostic factors;
- participants (country, number of participants, age, gender, type of stroke, time since stroke onset to study entry);
- inclusion and exclusion criteria;
- details of interventions in treatment and control groups;
- outcomes; and
- time points of measurement.

We tried to establish all unclear characteristics of the studies by contacting the trial co-ordinator or principal investigator. We checked the extracted data for agreement between authors and entered the data into Review Manager 5 (RevMan 5).

Assessment of risk of bias in included studies

We used the risk of bias assessment tool according to Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) to assess the adequacy of methods for sequence generation, concealment of allocation, ITT analysis, and blinding of assessors.

Furthermore, we used the PEDro scale, with 11 criteria, for methodological assessment of the included studies (Maher 2003). The PEDro scale assesses:

- specified eligibility criteria;
- random allocation;
- concealed allocation;
- similarity of baseline characteristics of the patients;
- blinding of patients;
- blinding of therapists;
- blinding of assessors;
- outcome data of at least 85% of participants of at least one key outcome;

- ITT analysis;
- between-group statistical comparisons; and
- point measures and measures of variability.

We scored each fulfilled criteria in the PEDro scale except the first one (specified eligibility criteria) with one point. Therefore, the maximum possible score was 10 points. Two review authors (HT and CD) independently assessed the PEDro scale of included studies. Because one author (CD) is principal investigator of an included trial, another author (JB) did the quality assessment of this study. We resolved disagreements in methodological assessment by consulting a third review author (MP or JB) and reached consensus through discussion. If an article did not contain information on any methodological criteria, we contacted the study authors for additional information. If no further information was available, we rated the criteria as 'unclear'.

Measures of treatment effect

The primary and secondary outcome variables of interest were continuous outcomes. We entered data of post-intervention assessment and follow-up assessment at six months as means and standard deviations (SDs) and calculated the standardised mean difference (SMD) with 95% confidence intervals (CIs) for each trial. We pooled data through calculation of the overall SMD and 95% CI. However, if post-intervention data were not available we used changes between pre- and post-assessment and summarised them in a separate analysis using the SMD and 95% CIs.

Unit of analysis issues

We considered randomised cross-over trials prior to cross-over and analysed only the first intervention phase.

Dealing with missing data

We contacted study authors if appropriate data for analysis were not adequately reported. If authors did not respond within one month after contact, we tried to get in contact with them at least one more time. We considered an ITT analysis as part of the risk of bias assessment.

Assessment of heterogeneity

We evaluated clinical heterogeneity through reported clinical and methodological diversity, variability of participants, interventions and outcomes in an additional table. The variability did not influence pooling trials. However, we used the I^2 statistic to quantify heterogeneity (cut-off 50%) for all comparisons. If we found substantial heterogeneity, we used a random-effects model instead of a fixed-effect model.

Assessment of reporting biases

We tried to minimise reporting bias through an extensive search of databases, handsearching of references lists and conference abstracts, and by contacting authors, trialists and experts in the field for other unpublished or ongoing trials. Furthermore, we conducted a sensitivity analysis, excluding studies of low methodological quality.

Data synthesis

Where possible, we conducted a pooled analysis of primary (motor function) and secondary (activities of daily living, pain, visuospatial neglect) outcomes as described above, using a random-effects model instead of a fixed-effect model if heterogeneity of the studies was high. We performed a subgroup analysis to establish the effectiveness relative to upper or lower extremity and type of control intervention. We also analysed subgroups by separating immediate and long-term results of mirror therapy.

Sensitivity analysis

To test the robustness of the results we conducted a sensitivity analysis, removing studies that we assessed to be of lower or ambiguous methodological quality (all studies with total PEDro scores less than seven points, all studies without adequate methods of sequence generation, concealment of allocation, ITT analysis and blinded assessors). We also reanalysed the data by removing cross-over RCTs.
Based on the inclusion criteria of the studies, we found two studies (Cacchio 2009a; Cacchio 2009b) that only included stroke patients with a diagnosis of CRPS-type I as defined by Bruehl 1999. One could argue that this is a special stroke population selected by a prominent feature. Furthermore, studies reported positive effects of mirror therapy in populations with CRPS of different origin (Ezendam 2009). This fact may influence the effects of mirror therapy in stroke patients with this feature. Therefore, we performed a post-hoc sensitivity analysis of the data without these two studies for all outcome measures.

R E S U L T S

Description of studies

See: Characteristics of included studies, Characteristics of excluded studies, Characteristics of studies awaiting classification, Characteristics of ongoing studies and Table 1.

Results of the search

We identified 19 studies from the search of the Cochrane Stroke Group's Trials Register. After excluding all duplicate references we identified a total of 1802 references from the other databases. Two review authors (HT and CD) identified 155 possible eligible trials. We excluded 140 studies. In the Excluded studies section, only those studies are mentioned that might in a superficial view appear to meet the eligibility criteria and those studies that were classified to be well known and likely to be considered relevant by some readers (Characteristics of excluded studies). There was insufficient information to determine inclusion eligibility for one trial (Amimoto 2008), but we failed to get in contact with the authors, therefore the study is listed as "awaiting classification" (see Characteristics of studies awaiting classification). Additionally, we identified four ongoing trials (see Characteristics of ongoing studies).

Included studies

Fourteen trials met the inclusion criteria of our review (Acerra 2007; Altschuler 1999; Cacchio 2009a; Cacchio 2009b; Dohle 2009; Ietswaart 2011; Manton 2002; Michielsen 2011; Rothgangel 2004; Seok 2010; Sütbeyaz 2007; Tezuka 2006; Yavuzer 2008; Yun 2010) (see Characteristics of included studies). We found two separate reports of one study (Rothgangel 2004; Rothgangel 2007) and based our data extraction and analysis on their first publication (Rothgangel 2004). One study was only available as an abstract (Manton 2002) and we were not able to contact the authors of the study and therefore had insufficient data to include this trial in the pooled analysis.

Design

Twelve studies were RCTs with parallel group design (Acerra 2007; Cacchio 2009a; Cacchio 2009b; Dohle 2009; Ietswaart 2011; Manton 2002; Michielsen 2011; Rothgangel 2004; Seok 2010; Sütbeyaz 2007; Yavuzer 2008; Yun 2010) and two studies used a cross-over design with random allocation to the order of treatment (Altschuler 1999; Tezuka 2006). For the latter two studies, we only used data of the first intervention period for pooled analysis.

Sample Size

The 14 studies included a total of 567 participants. Individual sample sizes of identified trials ranged from nine (Altschuler 1999) to 121 (Ietswaart 2011). A detailed description of individual sample sizes can be found in the Characteristics of included studies section.

Participants

Detailed descriptions of patient characteristics are given in Table 1.

The mean age of participants in the included studies ranged from 51 years (Seok 2010) to 79 years (Rothgangel 2004). There were more participants with a hemiparesis of the left side (55%). There were more male (57%) than female (43%) participants. One study did not provide data of participants (Manton 2002). Nine studies included participants after their first-ever stroke (Acerra 2007; Cacchio 2009a; Cacchio 2009b; Dohle 2009; Michielsen 2011; Rothgangel 2004; Sütbeyaz 2007; Yavuzer 2008; Yun 2010). Mean time post-stroke ranged between five days (Acerra 2007) and five years (Altschuler 1999). Four studies included participants in the acute or subacute phase after stroke (within three months post-stroke) (Acerra 2007; Dohle 2009; Tezuka 2006; Yun 2010) and eight trials included the chronic phase (more than three months) (Altschuler 1999; Cacchio 2009a; Cacchio 2009b; Manton 2002; Michielsen 2011; Rothgangel 2004; Sütbeyaz 2007; Yavuzer 2008). Two studies included participants within six months post-stroke (Ietswaart 2011; Seok 2010). Ten studies provided information on the aetiology of strokes; four studies did not (Altschuler 1999; Ietswaart 2011; Manton 2002; Seok 2010). Among those patients with known aetiology, 83% had an ischaemic and 17% a haemorrhagic stroke.

Twelve studies provided information of the study setting: inpatient rehabilitation (Acerra 2007; Dohle 2009; Seok 2010; Sütbeyaz 2007; Tezuka 2006; Yavuzer 2008; Yun 2010); inpatient and outpatient rehabilitation (Cacchio 2009a); day hospital and inpatient rehabilitation (Rothgangel 2004); home setting (Manton 2002; Michielsen 2011); and inpatient hospital and home setting (Ietswaart 2011). The included studies were conducted in nine different countries.

Studies used the following inclusion criteria.

- First-ever diagnosed stroke (Acerra 2007; Cacchio 2009a; Cacchio 2009b; Dohle 2009; Michielsen 2011; Rothgangel 2004; Sütbeyaz 2007; Yavuzer 2008; Yun 2010).
- Diagnosed stroke (Altschuler 1999; Ietswaart 2011; Seok 2010; Tezuka 2006).
- Diagnosis of CRPS-type I (Cacchio 2009a; Cacchio 2009b).
- Between 25 and 80 years of age (Dohle 2009).
- Able to follow therapy instructions (Dohle 2009; Seok 2010; Yavuzer 2008).
- Capable of participating in 30 minutes of daily therapy (Dohle 2009).
- Knowledge of Dutch language (Michielsen 2011).
- Ambulatory before stroke (Sütbeyaz 2007).
- Brunnstrom score between III and V (Michielsen 2011), between II and V (Seok 2010) or between I and IV (Yavuzer 2008; Yun 2010) for the upper extremity; between I and III (Sütbeyaz 2007) for the lower extremity.
- Minimal score of 1 on the Action Research Arm Test (Rothgangel 2004) or between 3 and 51 on the Action Research Arm Test (Ietswaart 2011).
- Grade of hemiparesis of 6 or less points after Ueda's method

(0 to 12 points) (Tezuka 2006).

- Home dwelling status (Michielsen 2011).

Studies used the following exclusion criteria.

- Major haemorrhagic changes, increased intracranial pressure and hemicraniectomy (Dohle 2009).
- Major comorbidities (Acerra 2007) or serious uncontrolled medical conditions (Cacchio 2009a; Cacchio 2009b; Yun 2010).
- Psychological diagnosis or cognitive impairment (e.g. severe dementia) that might interfere with study participation (Acerra 2007; Cacchio 2009a; Cacchio 2009b; Ietswaart 2011; Seok 2010; Sütbeyaz 2007; Yavuzer 2008; Yun 2010) or higher brain dysfunction (Tezuka 2006).
- Unco-operative patients (Yun 2010).
- Evidence of recent drug or alcohol abuse (Cacchio 2009a; Cacchio 2009b; Ietswaart 2011).
- Impairment of vision or hearing or both (Acerra 2007; Cacchio 2009a; Cacchio 2009b; Rothgangel 2004).
- Global aphasia (Cacchio 2009a; Cacchio 2009b).
- Severe aphasia (Ietswaart 2011; Seok 2010).
- Severe neglect (Michielsen 2011; Rothgangel 2004).
- Neglect, aphasia or apraxia (Yun 2010).
- Inability to sit supported for less than one hour (Acerra 2007).
- Other reasons for not being able to use the affected or unaffected limbs other than current stroke (Acerra 2007; Dohle 2009; Michielsen 2011).
- Musculoskeletal or neurological damage of the unaffected upper extremity (Seok 2010).
- Prior surgery to shoulder or neck or both (Cacchio 2009a; Cacchio 2009b).
- Intra-articular injection into the affected shoulder in the previous four months (Cacchio 2009a; Cacchio 2009b).
- Presence of other explanation for pain (Cacchio 2009a; Cacchio 2009b).
- Discharge from hospital within one week after admission (Ietswaart 2011).
- No upper limb motor weakness (Ietswaart 2011).
- Limited rehabilitation potential (Ietswaart 2011).
- Modified Ashworth Scale of three or more points (Seok 2010).

Seven studies reported no drop-outs during the intervention period (Acerra 2007; Altschuler 1999; Cacchio 2009b; Rothgangel 2004; Sütbeyaz 2007; Yavuzer 2008; Yun 2010), three trialists reported drop-out rates of less than 15% (Cacchio 2009a; Ietswaart 2011; Michielsen 2011) and in two studies the drop-out rate was above 15% (Dohle 2009; Tezuka 2006). In two studies the drop-out rate was unclear (Manton 2002; Seok 2010).
A total of 15 participants dropped out in the experimental groups and 11 participants dropped out in the control groups. Reasons for dropping out during mirror therapy were:

- death (Ietswaart 2011);
- moving to another city (Cacchio 2009a);
- changing hospital (Cacchio 2009a; Dohle 2009);
- worsening medical condition (Dohle 2009; Ietswaart 2011; Michielsen 2011);
- early discharge from rehabilitation (Dohle 2009);
- withdrawal of consent (Dohle 2009; Ietswaart 2011; Michielsen 2011; Tezuka 2006); and
- social issues (Michielsen 2011).

A detailed description of study characteristics can be found in the Characteristics of included studies section and in Table 1.

Interventions

Characteristics of interventions are summarised in Table 2. All included studies provided mirror therapy using a mirror or a mirror box in the midsagittal plane between the upper (Acerra 2007; Altschuler 1999; Cacchio 2009a; Cacchio 2009b; Dohle 2009; Manton 2002; Michielsen 2011; Rothgangel 2004; Seok 2010; Tezuka 2006; Yavuzer 2008; Yun 2010) or lower limbs (Sütbeyaz 2007). Thus, the mirror reflected movements of the non-affected side as if these movements were executed with the affected side.
Two studies used a combination of mirror therapy and other interventions. Yun 2010 integrated a second intervention group, in which mirror therapy was combined with neuromuscular electrical stimulation. We combined both intervention groups of this study for analysis using raw data. Ietswaart 2011 used mirror therapy within a motor imagery intervention protocol. Mirror therapy was integrated in this study to evoke action stimulation and was used during less than 10% of the total intervention duration.
Mirror therapy was provided for one to two (Ietswaart 2011), five (Cacchio 2009a; Cacchio 2009b; Dohle 2009; Michielsen 2011; Seok 2010; Sütbeyaz 2007; Yavuzer 2008; Yun 2010) or seven (Acerra 2007; Cacchio 2009b; Tezuka 2006) days a week for two (Acerra 2007) to six weeks (Dohle 2009; Michielsen 2011). Each session lasted between 10 (Ietswaart 2011; Tezuka 2006) and 60 minutes (Cacchio 2009a; Michielsen 2011). For one study (Manton 2002) a detailed description of the interventions could not be identified.
Rothgangel 2004 included a total of 16 participants and randomised them to mirror therapy or bilateral arm training. However, six of the patients were treated in an outpatient rehabilitation centre, and 10 in an inpatient care facility, which led to a significant difference in treatment time: the outpatient group received 17 treatment sessions, 30 minutes each; the inpatient group received 37 treatment sessions, 30 minutes each. Because these two groups are considerably different in total treatment time, we decided to analyse them separately (outpatient group: Rothgangel 2004a and inpatient group: Rothgangel 2004b).
In five studies participants performed bilateral movements, moving the affected limb behind the mirror as best they could (Acerra 2007; Altschuler 1999; Dohle 2009; Michielsen 2011; Yavuzer 2008). In six studies patients only moved the unaffected side while

looking in the mirror (Cacchio 2009a; Cacchio 2009b; Ietswaart 2011; Seok 2010; Sütbeyaz 2007; Yun 2010). In the study of Rothgangel 2004 patients with muscle hypotonia had to move the affected arm as best they could; patients with muscle hypertonia should only move the unaffected arm while looking into the mirror. In one study, a therapist passively moved the affected arm behind the mirror according to the movements of the unaffected one (Tezuka 2006).

Control interventions of all included studies were carried out with the same amount and frequency as the experimental intervention, except for one study (Seok 2010), where the control group received no additional intervention to standard rehabilitation. Ietswaart 2011 included two control groups, where the second control group received no additional treatment to normal care. Five studies used a form of sham therapy (Acerra 2007; Cacchio 2009a; Cacchio 2009b; Sütbeyaz 2007; Yavuzer 2008) where the reflecting side of the mirror was covered, or the nonreflecting side of the mirror was placed in the direction of the unaffected arm while practising. Yun 2010 included a control group with neuromuscular electrical stimulation but also with a covered mirror between limbs. Four studies provided interventions with an unrestricted view on the affected side using the same training as in the experimental groups but without a mirror (Dohle 2009; Michielsen 2011; Rothgangel 2004) or with a plexiglas between limbs (Altschuler 1999). In one study a therapist passively moved the affected arm according to the movements of the unaffected one but without a mirror between limbs (Tezuka 2006). Cacchio 2009b included a second control group, practising motor imagery tasks. We combined the two control groups of this study for overall analysis. As mentioned above, Ietswaart 2011 included two control groups, where the first control group received an attention-placebo intervention. Patients in this group performed mental rehearsal that was not related to motor control. We combined both control groups of this study for analysis.

Based on the difference of using a covered mirror or no mirror (also transparent plexiglas), we performed a subgroup analysis differentiating the effects of both types of control intervention (covered mirror versus unrestricted view).

Outcome

The included studies used a number of different outcomes. A description of the outcome measures used can be found in Characteristics of included studies.

Primary outcome: motor function

For analysis of our primary outcome motor function we used the Fugl-Meyer score of the upper extremity (Dohle 2009; Michielsen 2011; Yun 2010) or wrist and fingers (Tezuka 2006), the Action Research Arm Test (Ietswaart 2011; Rothgangel 2004), the Wolf Motor Function Test (functional ability) (Cacchio 2009a; Cacchio 2009b), the Motor Assessment Scale Item 7 (Acerra 2007) and the Brunnstrom stages of motor recovery lower extremity (Sütbeyaz 2007) or upper extremity and hand (combined using raw data) (Yavuzer 2008).

Secondary outcomes: activities of daily living, pain and visuospatial neglect

In our pooled analysis of the secondary outcome activities of daily living we used the Functional Independence Measure motor subscore (Dohle 2009; Sütbeyaz 2007) or self-care subscore (Yavuzer 2008) and the Barthel Index (Ietswaart 2011). For the analysis of the secondary outcome of pain we included the measurement of pain at rest (Acerra 2007; Cacchio 2009b; Michielsen 2011) and during movement (Cacchio 2009a; Dohle 2009). The investigators used Numerical Rating Scales (Acerra 2007) between 0 and 10, Visual Analogue Scales between 0 and 10 (Cacchio 2009a) or between 0 mm and 100 mm (Cacchio 2009b; Michielsen 2011) or the pain section of the Fugl-Meyer Assessment, normalised on the average score per item (0 to 2; 2 indicating no pain) (Dohle 2009).

Visuospatial neglect as an outcome was included in one study (Dohle 2009). The authors used a self-defined five-point neglect score based on the Behavioral Inattention Test (BIT) and the Test of Attentional Performance (TAP).

Follow-up assessment

Seven studies provided follow-up assessments of one month (Acerra 2007), five weeks (Rothgangel 2004), three months (Manton 2002) and six months (Cacchio 2009a; Michielsen 2011; Sütbeyaz 2007; Yavuzer 2008) after the intervention period. For analysis of sustained treatment effects for our primary outcome, we used only the data of follow-up assessments after six months.

Adverse effects

Only one study explicitly reported the assessment of adverse effects (Acerra 2007).

Excluded studies

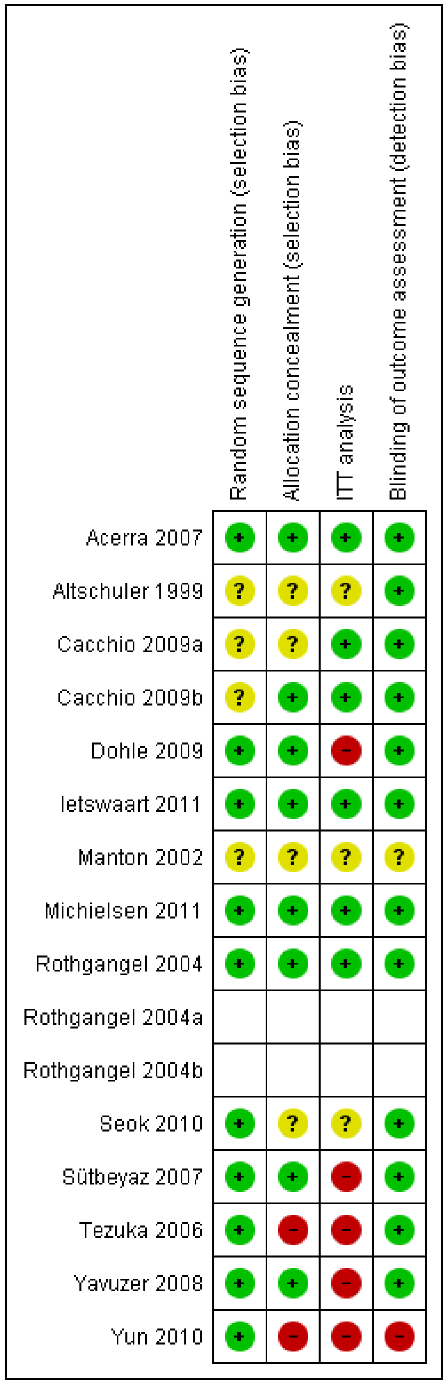
We excluded a total of 140 studies following consideration of abstracts, full texts or both (see: Characteristics of excluded studies section). Clinical studies with stroke patients employing computer graphic implementation of mirror therapy were generally not RCTs (Gaggioli 2009; Merians 2009).

Risk of bias in included studies

All details about the methodological quality of the included studies using the risk of bias assessment tool (Higgins 2011) and the

PEDro Scale are provided in Characteristics of included studies, Figure 1, and Table 3.

Figure 1. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



We emailed all trialists of the included studies to clarify some methodological or design issues, or both. Most trialists provided at least some of the requested information. We did not receive an answer to methodological issues for three trials (Altschuler 1999; Manton 2002; Seok 2010).
Two review authors (HT and CD) independently evaluated the methodological quality of the studies using the PEDro scale. One trial was rated by JB instead of CD. The review authors disagreed on the criteria of:

- baseline comparability (Altschuler 1999; Dohle 2009);
- adequate follow-up assessment (Altschuler 1999); and
- ITT analysis (Altschuler 1999; Dohle 2009; Michielsen 2011; Rothgangel 2004; Sütbeyaz 2007; Yavuzer 2008).

The assessing authors discussed all disagreements and resolved them by contacting another author or obtaining additional information through contact with the principal investigator of the study. Table 3 presents the ratings of each item and the total score of the PEDro scale of the included studies. In general, the quality of studies could be regarded as high. As it is not possible to blind patients and therapists to the intervention, the maximum possible total score is 8 out of 10 points. Three of the included studies reached the maximum possible score of eight points (Acerra 2007; Cacchio 2009b; Michielsen 2011). The study by Manton 2002 only reached a total score of one point due to incomplete information. The median possible PEDro score of all included studies was seven points.

Allocation

Two studies used a cross-over design with random allocation to the order of treatment (Altschuler 1999; Tezuka 2006). We only analysed the first treatment period as a parallel group design in these two studies. Three studies used block randomisation methods (Cacchio 2009b; Sütbeyaz 2007; Yavuzer 2008). One study (Ietswaart 2011) based their randomised group allocation on different stratification factors. Another study randomly allocated ability matched pairs to treatment groups (Manton 2002). Eight studies used a concealment of allocation (Acerra 2007; Cacchio 2009b; Dohle 2009; Ietswaart 2011; Michielsen 2011; Rothgangel 2004; Sütbeyaz 2007; Yavuzer 2008).

Blinding

In all but two studies (Manton 2002; Yun 2010), at least the primary outcome measures were assessed by people blinded to group allocation.

Other potential sources of bias

The methods used for concealment of allocation are presented in the Characteristics of included studies tables. An ITT analysis was performed in six studies (Acerra 2007; Cacchio 2009a; Cacchio 2009b; Ietswaart 2011; Michielsen 2011; Rothgangel 2004).
Information about the reasons for dropping out are presented in the Characteristics of included studies section. Only one of the included studies explicitly reported that they found no adverse effects (Acerra 2007).

Effects of interventions

We included 13 studies with a total of 506 participants in the analysis (Acerra 2007; Altschuler 1999; Cacchio 2009a; Cacchio 2009b; Dohle 2009; Ietswaart 2011; Michielsen 2011; Rothgangel 2004; Seok 2010; Sütbeyaz 2007; Tezuka 2006; Yavuzer 2008; Yun 2010). Rothgangel 2004 provided data on two subgroups of patients. Because these two subgroups are considerably different in total treatment time, we analysed them separately (subgroup 1: Rothgangel 2004a and subgroup 2: Rothgangel 2004b). One included study was only available as an abstract and did not provide sufficient data for analysis (Manton 2002).

Comparison 1: Mirror therapy versus all other interventions

Outcome 1.1: Motor function at the end of the intervention phase

We included 13 studies in a pooled analysis on motor function after study end (Acerra 2007; Altschuler 1999; Cacchio 2009a; Cacchio 2009b; Dohle 2009; Ietswaart 2011; Michielsen 2011; Rothgangel 2004; Seok 2010; Sütbeyaz 2007; Tezuka 2006; Yavuzer 2008; Yun 2010). As two studies (Altschuler 1999; Rothgangel 2004) only presented change scores between pre- and post-assessment, we performed separate analyses for post-assessment data and changes between pre- and post-assessment, to control for possible differences in study effects.
We included eleven studies with a total of 234 participants in the intervention and 247 in the control groups in the post-assessment data analysis (Acerra 2007; Cacchio 2009a; Cacchio 2009b; Dohle 2009; Ietswaart 2011; Michielsen 2011; Seok 2010; Sütbeyaz 2007; Tezuka 2006; Yavuzer 2008; Yun 2010). Mirror therapy has a significant effect on motor function in patients after stroke compared with all other types of interventions (SMD 0.61; 95% CI 0.22 to 1.0; P = 0.002; I^2 = 75%, random-effects model) (Analysis 1.1).

Nine studies with a total of 147 participants in the intervention and 136 in the control groups provided change scores between pre- and post-assessment (Altschuler 1999; Cacchio 2009a; Cacchio 2009b; Rothgangel 2004; Seok 2010), or we used raw data for analysis of change scores (Dohle 2009; Tezuka 2006; Yavuzer 2008; Yun 2010). In the analysis of change scores, we also found a significant effect of mirror therapy compared with all other interventions on motor function after stroke (SMD 1.04; 95% CI 0.57 to 1.51; $P < 0.0001$; $I^2 = 65\%$, random-effects model) (Analysis 1.1).

Because the effects based on change scores might be overestimated, and only two studies with a total of 25 participants presented change scores (Altschuler 1999; Rothgangel 2004), we based all further analysis on studies that provided post-intervention data.

Outcome 1.2: Activities of daily living at the end of the intervention phase

We included four studies in the analysis of the outcome of activities of daily living (Dohle 2009; Ietswaart 2011; Sütbeyaz 2007; Yavuzer 2008). These studies included 94 participants in the intervention and 123 in the control groups. Mirror therapy has a significant effect on activities of daily living for patients with stroke, compared with all other interventions (SMD 0.33; 95% CI 0.05 to 0.60; $P = 0.02$; $I^2 = 15\%$, fixed-effect model) (Analysis 1.2).

Outcome 1.3: Pain at the end of the intervention phase

For analysing the effects of mirror therapy on pain at the end of the intervention, we included five studies presenting data on pain at rest or during movement (Acerra 2007; Cacchio 2009a; Cacchio 2009b; Dohle 2009; Michielsen 2011). These five studies included 90 participants in the intervention and 98 in the control groups. Mirror therapy has a significant effect on pain reduction for patients after stroke, compared with all other interventions (SMD -1.10; 95% CI -2.10 to -0.09; $P = 0.03$; $I^2 = 89\%$, random-effects model) (Analysis 1.3).

Outcome 1.4: Visuospatial neglect at the end of the intervention

One study reported outcome on visuospatial neglect (Dohle 2009). They presented data only on those patients who initially presented a visuospatial neglect (9 in the intervention and 11 in the control group). Based on these data, we found a significant effect of mirror therapy versus all other interventions on visuospatial neglect after stroke (SMD 1.22; 95% CI 0.24 to 2.19) (Analysis 1.4)

Outcome 1.5: Motor function at follow-up after six months

Four studies provided data on motor function at a follow-up period of six months (Cacchio 2009a; Michielsen 2011; Sütbeyaz 2007; Yavuzer 2008). These studies included 78 patients in the experimental and 79 in the control groups. At follow-up after six months, mirror therapy had a significant, lasting effect on motor function in patients after stroke, compared with all other interventions (SMD 1.09; 95% CI 0.30 to 1.87; $P = 0.007$; $I^2 = 81\%$, random-effects model) (Analysis 1.5).

No adverse events of mirror therapy were reported.

Comparison 2: Subgroup analysis - upper versus lower extremity

Outcome 2.1: Motor function at the end of the intervention phase

We performed a subgroup analysis for those studies examining mirror therapy for the upper extremity (subgroup 2.1.1) and lower extremity (subgroup 2.1.2) (Analysis 2.1). Thirteen studies examined mirror therapy for the upper extremity. Of these studies, we could include post-intervention data of 10 studies with 194 participants in the experimental and 227 in the control groups (Acerra 2007; Cacchio 2009a; Cacchio 2009b; Dohle 2009; Ietswaart 2011; Michielsen 2011; Seok 2010; Tezuka 2006; Yavuzer 2008; Yun 2010). We found a significant effect of mirror therapy on motor function of the upper extremity for patients after stroke compared to all other interventions (SMD 0.53; 95% CI 0.04 to 1.01; $P = 0.03$; $I^2 = 82\%$, random-effects model) (Analysis 2.1).

One study with 20 participants in the experimental and control groups examined mirror therapy for the lower extremity (Sütbeyaz 2007). The effect of mirror therapy on motor function of the lower extremity for patients after stroke compared with all other interventions just reached significance (SMD 0.65; 95% CI 0.01 to 1.29; $P = 0.05$) (Analysis 2.1).

Comparison 3: Subgroup analysis - sham intervention (covered mirror) versus other intervention (unrestricted view)

We found two different groups of control interventions. In all studies, participants in the control group performed the same movements as participants in the experimental groups. However, in one type of control intervention, the view on the affected side was obscured with a covered mirror, or with the non-reflective side of the mirror (sham intervention). In the other type of control intervention, participants had an unrestricted view on both; the unaffected and the affected limb (other intervention). Because we believed that this may have influenced the effect of therapy, we performed a subgroup analysis, differentiating these two types of studies.

Outcome 3.1: Motor function at the end of the intervention phase

Six studies used a covered mirror in the control group (Acerra 2007; Cacchio 2009a; Cacchio 2009b; Sütbeyaz 2007; Yavuzer 2008; Yun 2010). These studies included 129 participants in the intervention and 111 in the control groups. For this subgroup we found a significant effect of mirror therapy on motor function after stroke (SMD 0.90; 95% CI 0.27 to 1.52; P = 0.005; I^2 = 79%, random-effects model). Five studies used no mirror, or a transparent plexiglas in the control groups, thus providing a view of both limbs (Altschuler 1999; Dohle 2009; Michielsen 2011; Rothgangel 2004; Tezuka 2006); we could analyse three of these studies. These studies included 47 participants in the experimental and 44 in the control groups. The effect of mirror therapy on motor function after stroke in these studies just reached significance (SMD 0.42; 95% CI 0.00 to 0.84; P = 0.05; I^2 = 0%). However, the difference between subgroups was not statistically significant (P = 0.22) (Analysis 3.1).

Comparison 4: Sensitivity analysis by trial methodology

We tested the robustness of the results by analysing only RCTs and excluding randomised cross-over trials, and by using specific methodological variables that could influence the observed treatment effects (PEDro total score > 6 points, concealment of allocation, blinding of assessors and ITT analysis) (Analysis 4.1).

Outcome 4.1: Motor function at the end of the intervention phase

All studies without randomised cross-over trials

We classified 12 studies as RCTs, of which we included 10 in a subgroup analysis of all studies without randomised cross-over trials (Acerra 2007; Cacchio 2009a; Cacchio 2009b; Dohle 2009; Ietswaart 2011; Michielsen 2011; Seok 2010; Sütbeyaz 2007; Yavuzer 2008; Yun 2010). The studies included 225 participants in the experimental and 241 in the control groups. Based on the analysis, mirror therapy has a significant effect on motor function in patients after stroke, compared to all other treatments (SMD 0.59; 95% CI 0.18 to 1.0; P = 0.005; I^2 = 77%, random-effects model) (Analysis 4.1).

All studies with a PEDro total score greater than 6 points

We classified eight studies as having more than six points in the PEDro scale, of which we could integrate seven in a pooled analysis (Acerra 2007; Cacchio 2009a; Cacchio 2009b; Ietswaart 2011; Michielsen 2011; Sütbeyaz 2007; Yavuzer 2008). The studies included 148 participants in the experimental and 182 in the control groups. We found a significant effect of mirror therapy, compared with all other therapies for patients after stroke (SMD 0.81; 95% CI 0.27 to 1.36; P = 0.004; I^2 = 81%, random-effects model) (Analysis 4.1).

All studies with adequate sequence generation

We classified 10 studies as having an adequate method of sequence generation. We analysed nine studies with 202 participants in the intervention and 207 in the control groups (Acerra 2007; Dohle 2009; Ietswaart 2011; Michielsen 2011; Seok 2010; Sütbeyaz 2007; Tezuka 2006; Yavuzer 2008; Yun 2010). We found a significant effect of mirror therapy compared with all other therapies for patients after stroke (SMD 0.31; 95% CI 0.09 to 0.54; P = 0.007; I^2 = 18%) (Analysis 4.1).

All studies with adequate concealed allocation

We classified seven studies as having used an adequate method of allocation concealment. We analysed six studies with 134 participants in the experimental and 160 in the control groups (Acerra 2007; Dohle 2009; Ietswaart 2011; Michielsen 2011; Sütbeyaz 2007; Yavuzer 2008). Based on the analysis, we found a significant effect of mirror therapy compared with all other therapies for patients after stroke (SMD 0.39; 95% CI 0.12 to 0.66; P = 0.005; I^2 = 23%) (Analysis 4.1).

All studies with adequate intention-to-treat (ITT) analysis

We classified six studies as having used an adequate ITT analysis. Based on our analysis of five studies (Acerra 2007; Cacchio 2009a; Cacchio 2009b; Ietswaart 2011; Michielsen 2011) with 111 participants in the experimental and 143 in the control groups with post-intervention data, mirror therapy has a significant effect on motor function compared with all other interventions (SMD 0.91; 95% CI 0.12 to 1.71; P = 0.02; I^2 = 87%, random-effects model) (Analysis 4.1).

All studies with blinded assessors

Twelve studies used blinded assessors for at least the primary outcome. In this analysis we included 10 studies with 194 participants in the experimental and 227 in the control groups (Acerra 2007; Cacchio 2009a; Cacchio 2009b; Dohle 2009; Ietswaart 2011; Michielsen 2011; Seok 2010; Sütbeyaz 2007; Tezuka 2006; Yavuzer 2008). Mirror therapy has a significant positive effect on motor function compared with all other interventions (SMD 0.67; 95% CI 0.25 to 1.10; P = 0.002; I^2 = 76%, random-effects model) (Analysis 4.1).

Comparison 5: Post-hoc sensitivity analysis - removing studies that only included studies with complex regional pain syndrome (CRPS) after stroke

Two studies (Cacchio 2009a; Cacchio 2009b) only included patients after stroke with a diagnosis of CRPS-type I which might have influenced the effects of the intervention. Thus, we performed a post-hoc sensitivity analysis and removed studies that only included participants with CRPS after stroke.

Outcome 5.1: Motor function at the end of the intervention phase

We included 11 studies, of which we analysed nine (Acerra 2007; Dohle 2009; Ietswaart 2011; Michielsen 2011; Seok 2010; Sütbeyaz 2007; Tezuka 2006; Yavuzer 2008; Yun 2010). These nine studies included 202 participants in the intervention and 207 in the control groups. Excluding those studies that only included patients with CRPS led to a reduced, but still significant effect of mirror therapy on motor function for patients after stroke, compared with all other interventions (SMD 0.31; 95% CI 0.09 to 0.54; P = 0.0007; I^2 = 18%) (Analysis 5.1).

Outcome 5.2: Pain at the end of the intervention phase

After removing those two studies that only included patients with CRPS, we included three studies with 58 participants in the intervention and 58 in the control groups (Acerra 2007; Dohle 2009; Michielsen 2011). We found no significant effect on pain for mirror therapy compared with all other interventions in this subgroup (SMD -0.16; 95% CI -0.53 to 0.20; P = 0.38; I^2 = 0%) (Analysis 5.2)

Outcome 5.3: Motor function at follow-up after six months

We removed one study that included stroke patients with CRPS only. We analysed three studies with 54 participants in the experimental and 55 in the control group (Michielsen 2011; Sütbeyaz 2007; Yavuzer 2008). We found a reduced, but still significant effect of mirror therapy compared with all other interventions for motor function at follow-up after six months (SMD 0.69; 95% CI 0.26 to 1.13; P = 0.002; I^2 = 18%).

DISCUSSION

Summary of main results

The main purpose of this review was to evaluate the effect of mirror therapy for improving motor function, activities of daily living and reducing pain and visuospatial neglect for patients after stroke. We included 14 studies (12 RCTs and two randomised cross-over studies), with a total of 567 participants that compared mirror therapy with other interventions. We found evidence that mirror therapy may improve motor function, activities of daily living, pain and visuospatial neglect compared with all other interventions. Furthermore, the effects on motor function were stable at follow-up assessment after six months. No adverse events of mirror therapy were reported.

Thirteen of the included studies evaluated the effect of mirror therapy on the upper extremity, and one study evaluated the effect of mirror therapy on the lower extremity. Mirror therapy was effective in improving motor function, both for the upper extremity and for the lower extremity. Based on a subgroup analysis, we found evidence that the effects might have been influenced by the type of control treatment: effects on motor function were robustly significant in those studies that compared mirror therapy with a sham intervention that uses a covered mirror, thus avoiding any view of the affected limb. Significance was just reached and the overall effect was smaller in studies that used unrestricted view (no mirror or a transparent plexiglas). It should be noted that Cacchio 2009a and Cacchio 2009b only included patients with a diagnosis of complex regional pain syndrome (CRPS)-type I after stroke. By excluding these two studies in a sensitivity analysis however, the evidence that mirror therapy may improve motor function and motor function at six months follow-up remained. However, no significant effect on pain was present after excluding the studies of stroke patients with a diagnosed CRPS-type 1.

Quality of the evidence

We used several methodological domains (adequate sequence generation, adequate concealment of allocation, adequate ITT analysis and blinding of assessors) to assess the risk of bias in the included studies. We assessed four studies as having unclear sequence generation. Furthermore, we found six studies with no or unclear use of concealed allocation of participants to study groups, and eight studies with no or unclear use of an adequate ITT analysis. All but two analysed studies used blinded assessors. Additionally, we assessed the PEDro scale for evaluating the methodological quality of the studies (Maher 2003). The median of the PEDro scale total scores was seven points, indicating overall a high quality of studies. However, we classified six studies to have a PEDro score lower than seven points.

Some of the analysis showed significant heterogeneity. However, in all cases this was no longer present when leaving out those studies that included only patients with CRPS after stroke. However, we cannot exclude the possibility that other factors are responsible for the heterogeneity. Therefore, caution in the interpretation of the results is needed.

In order to test for potential biases through methodological issues, we performed a sensitivity analysis and excluded randomised cross-over studies, studies with a total PEDro score below seven points, studies with unclear adequacy of sequence generation, studies with inadequate concealment of allocation, studies not providing an ITT analysis and studies that did not use assessors blinded to intervention. Based on that sensitivity analysis, the effects of mirror therapy on motor function of patients after stroke were robust. However, overall limitations of the included studies were small sample sizes of most studies, very limited inclusion of control groups that used other effective interventions for the upper or lower extremity in most studies and differences in therapy delivery between the studies (i.e. amount and frequency of the treatment period).

Potential biases in the review process

Through an extensive searching process, we are confident that we have identified all relevant studies in the field. However, a risk of publication bias towards a selection of positive results remains. Furthermore, there is a small possibility of additional (published or unpublished) studies that we did not identify. As stated above, there was heterogeneity between studies in terms of trial design (i.e. parallel group and cross-over trials, duration of follow-up and selection criteria for patients), characteristics of patients (i.e. severity of motor impairment and time since stroke onset) and characteristics of interventions (i.e. total amount of time of therapy, percentage of the intervention dedicated to mirror therapy only and therapy for upper or lower extremity). We also identified methodological limitations of studies. However, as stated above, a sensitivity analysis with respect to methodological limitations and patient characteristics revealed the robustness of the results across all stated potential confounding factors.

Agreements and disagreements with other studies or reviews

The results of this review are in line with the results of other reviews (Ezendam 2009; Rothgangel 2011). These reviews were systematic in terms of their method. However, they had more limited search strategies, only included studies that were published before 2009 and did not use a pooled analysis of identified studies. A narrative review also described positive effects of mirror therapy after stroke (Ramachandran 2009).

Potential benefit

We found that mirror therapy was effective in terms of improving motor function of the upper extremity, activities of daily living and pain for patients that suffered a stroke. No conclusion could be drawn in terms of visuospatial neglect because the results were based on only one study with a small population. The positive results for motor function were consistent with follow-up assessment after six months. The results are limited because our subgroup analysis indicates evidence of a greater effect of mirror therapy on motor function when compared with a sham intervention (using a covered mirror) than when compared with other interventions (using unrestricted view). Therefore, the positive effects in this review at least indicate that mirror therapy as an adjunct to routine therapy can improve motor function for patients after stroke.

Mirror therapy did significantly reduce pain in patients after stroke. However, this result is mainly based on two studies that included only patients with CRPS-type I after stroke and should not be generalised to an unselected stroke patient population.

One of the potential advantages of mirror therapy compared with other interventions may be due to the possibility of training by moving the unaffected arm or both arms while looking in the mirror. Therefore, even patients with severe paresis could practise on their own without a therapist. Furthermore, mirror therapy could be applied at home as evaluated in two studies (Manton 2002; Michielsen 2011). However, we were not able to test the effectiveness of this therapy regime explicitly due to limited data.

AUTHORS' CONCLUSIONS

Implications for practice

The results of this review indicate that there is evidence for the effectiveness of mirror therapy for improving motor function for patients after stroke. The effects were more prominent and with a clear statistical significance when mirror therapy was compared with sham intervention. Compared with bilateral arm training with unrestricted view, the effects for mirror therapy only just reached significance. Therefore, mirror therapy could be applied as an additional intervention in the rehabilitation of patients after stroke, but no clear conclusion could be drawn if mirror therapy replaced other interventions for improving motor function of the arm. Additionally, we found evidence that mirror therapy may improve activities of daily living and visuospatial neglect, but the results must be interpreted with caution. Results for activities of daily living are based on only four studies. No clear implication could be drawn for visuospatial neglect, because results are based on only one study. Significant effects on pain are only present in studies that included only patients with a CRPS-type 1 after stroke. Therefore, for this subgroup of patients, mirror therapy seems to be an effective intervention, both for improving motor function and reducing pain.

Implications for research

There is a need for well designed randomised controlled studies with large sample sizes in order to evaluate the effects of mirror therapy after stroke. Above all, further research should compare mirror therapy with other conventionally applied or newly developed and effective therapies. Additionally, further research should address specific questions due to the optimal dose, frequency and duration of mirror therapy, and should focus on outcomes in activities of daily living. Further research should also answer questions about the effects of mirror therapy according to the extent of motor impairment, and should even focus on patients with impairments other than motor impairments after stroke, such as pain and visuospatial neglect. Finally, it is important to update this review regularly in order to include studies that are ongoing at the time of publication.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Acerra 2007

Methods	RCT
Participants	Country: Australia Sample size: 40 participants (20 in each group) Inclusion criteria: acute stroke (< 2 weeks) Exclusion criteria: previous stroke; vision or hearing impairment; acute trauma or impairment of the limbs; inability to sit for < 1 hour; MMSE < 22/30; major co-morbidities
Interventions	2 arms: 1. mirror therapy: participants were instructed to move both arms while looking in the mirror box, sensory stimulation 2. sham therapy: patients performed the same treatment protocol as in group 1 but only viewing the unaffected arm 1 and 2: 5 days a week, 20 to 30 minutes for 2 weeks; additional usual rehabilitation programme
Outcomes	Outcomes were recorded at baseline, after 2 weeks of treatment and 1 month after treatment • MAS (item 7 and 8, each 0 to 6) • Resting pain intensity (NRS 0 to 10); differential CRPS-type 1 diagnosis • grip strength (handheld dynamometer) • sensory detection (synchiria yes/no, QST) • adverse events
Notes	Unpublished data We used means and SDs of Item 7 of the MAS, and combined the scores on pain intensity of shoulder and hand

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated random number sequence
Allocation concealment (selection bias)	Low risk	Generated list was used by an independent person for group allocation
ITT analysis	Low risk	Results were analysed on an ITT basis
Blinding of outcome assessment (detection bias) primary outcome	Low risk	Assessors were blinded to group allocation

Altschuler 1999

Methods	Randomised cross-over trial
Participants	Country: USA Sample size: 9 participants (9 in each group) Inclusion criteria: at least 6 months post-stroke
Interventions	2 arms: 1. 4 weeks of mirror therapy: participants were instructed to move the non-paretic arm while looking in the mirror and moving the paretic arm as best they could; followed by 4 weeks of control therapy, using transparent plastic instead of a mirror 2. vice versa
Outcomes	Outcomes were recorded at baseline, after 2, 4, 6 and 8 weeks • self-developed scale (-3 to +3); assessing changes in patients' movement ability in terms of range of motion, speed and accuracy by video analysis
Notes	Data not included in the analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Patients were randomly assigned (authors' statement)
Allocation concealment (selection bias)	Unclear risk	Not stated
ITT analysis	Unclear risk	Not stated
Blinding of outcome assessment (detection bias) primary outcome	Low risk	Assessors were blinded to group allocation

Cacchio 2009a

Methods	RCT
Participants	Country: Italy Sample size: 48 participants (24 in each group; 6 dropped out post-treatment, 3 more dropped out after 6 months) Inclusion criteria: hemiparesis after first ever ischaemic or haemorrhagic stroke; during first 6 months post-stroke; diagnosed with CRPS-type 1 with a VAS pain score > 4 cm Exclusion criteria: an intra-articular injection into the affected shoulder during the previous 6 months or use of systemic corticosteroids during the previous 4 months; presence of another explanation of pain; prior surgery to shoulder or neck; serious uncontrolled medical conditions; global aphasia or cognitive impairments; visual impairments which might interfere with the aims of the study; evidence of recent alcohol or drug abuse; or severe depression

Interventions	2 arms: 4-week conventional stroke rehabilitation programme and additional 1. mirror therapy: participants performed upper extremity movements while looking in the mirror, without additional verbal feedback 2. sham therapy: patients performed the same treatment protocol as in group 1 but with covering the reflecting side of the mirror 1 and 2: 5 days a week, 30 minutes of therapy for the first 2 weeks; and 5 days a week, 60 minutes of therapy for the last 2 weeks
Outcomes	Outcomes were recorded at baseline, 1 week after the intervention period and after 6 months • WMFT/FA; 0 to 5, lower scores indicating better functioning • WMFT/PT; in seconds • QOM item in the MAL (0 to 5) • Pain at rest (VAS 0 to 10) • Pain on movement (VAS 0 to 10) • Pain tactile allodynia (VAS 0 to 10)
Notes	Published and unpublished data

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Patients were randomly allocated (authors' statement)
Allocation concealment (selection bias)	Unclear risk	Not stated
ITT analysis	Low risk	Results were analysed on an ITT basis
Blinding of outcome assessment (detection bias) primary outcome	Low risk	Assessors were blinded to group allocation

Cacchio 2009b

Methods	RCT
Participants	Country: Italy Sample size: 24 Participants (8 in each group) Inclusion criteria: first ischaemic or haemorrhagic stroke (> 6 months); diagnosis of CRPS-type 1 (pain VAS > 4 cm) Exclusion criteria: intra-articular shoulder injection in the previous 6 months or systemic corticosteroid in the previous 4 months; another obvious explanation for pain; prior surgery to shoulder or neck region; serious uncontrolled medical conditions; global aphasia or cognitive impairments interfering with understanding instructions, motor testing and treatment; visual impairments interfering with aims of the study; evidence of recent alcohol or drug abuse; or severe depression

Interventions	3 arms: 1. mirror therapy: participants performed cardinal upper extremity movements while looking in the mirror 2. sham therapy: patients performed the same treatment protocol as in group 1 but with covering the reflecting side of the mirror 3. mental imagery: participants performed mental imagery 1, 2 and 3: 5 days a week; 30 minutes of therapy for 4 weeks
Outcomes	Outcomes were recorded at baseline and after the intervention period • WMFT/FA: 0 to 5, lower scores indicating better functioning • WMFT/PT: in seconds • Pain (VAS 0 to 10) • Brushed induced allodynia • Oedema
Notes	Published and unpublished data; we only analysed the first intervention period (4 weeks) ; we summarised groups 2 and 3 to one control group

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Block randomisation; sequence generation method not stated
Allocation concealment (selection bias)	Low risk	A therapist not involved in the treatments; opened sealed envelopes and assigned appointments according to treatment group (authors' statement)
ITT analysis	Low risk	Results were analysed on an ITT basis
Blinding of outcome assessment (detection bias) primary outcome	Low risk	Assessors were blinded to group allocation

Dohle 2009

Methods	RCT
Participants	Country: Germany Sample size: 48 participants (24 in each group, 12 dropped out) Inclusion criteria: first ever ischaemic stroke in the territory of the middle cerebral artery; not more than 8 weeks post-stroke; between 25 and 80 years old; able to follow therapy instructions; capable of participating in 30-minute daily therapy sessions Exclusion criteria: experienced previous stroke; major haemorrhagic changes; increased intracranial pressure; hemicraniectomy or orthopedic, rheumatologic, or other diseases interfering with their ability to sit or to move either upper limb

Interventions	2 arms: 1. mirror therapy: participants were instructed to move both arms "as well as possible" while looking in the mirror 2. bilateral arm training: patients performed the same treatment protocol as in group 1 but without a mirror 1 and 2: 5 days a week; 30 minutes of therapy for 6 weeks
Outcomes	Outcomes were recorded at baseline and after the intervention • FM-UE motor, ROM, pain and sensory section (FM-UE 0 to 126) • ARAT 0 to 57 • FIM self-care and mobility items (7 to 77) • self-defined Neglect score (0 to 4)
Notes	Published and unpublished data; we extracted the motor section of the FM-UE (without reflex activity, 0 to 60)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Sealed, numbered envelopes were created
Allocation concealment (selection bias)	Low risk	Sealed envelopes were broken after study inclusion
ITT analysis	High risk	Drop-outs were not included in analysis
Blinding of outcome assessment (detection bias) primary outcome	Low risk	Assessors of primary outcome were blinded to group allocation

Ietswaart 2011

Methods	RCT
Participants	Country: Scotland, UK Sample size: 121 participants (experimental: 41; control 1: 39; control 2: 41; 18 dropped out) Inclusion criteria: stroke in the prior 1 to 6 months; ARAT score 3 to 51; no evidence of alcohol or substance abuse; no severe cognitive deficits - Mental Status Questionnaire > 6; no severe aphasia
Interventions	3 arms: 1. motor imagery: 30 minutes of mental practice of elementary movements, goal directed movements and ADL; 10 minutes mirror therapy or active motor using video (alternated between sessions); 5 minutes motor imagery 2. attention-placebo control: 25 minutes active visual and sensory imagery of non-motor tasks; 10 minutes of tasks for controlling cognitive inhibition; 5 minutes

	watching optical illusions; 5 minutes visual imagery of objects 3. standard care without additional intervention 1 and 2: 3 days a week; 45 minutes of therapy for 4 weeks additional to standard; additional 8 sessions of 30 minutes unsupervised motor imagery 1 or non-motor imagery 2
Outcomes	Outcomes were recorded at baseline and after 5 weeks: • ARAT (0 to 57) • BI • Grip strength (hand held dynamometer) • Timed manual dexterity performance • Modified functional limitation profile
Notes	Only 8% of the intervention included mirror therapy as defined in the review

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Automated randomisation procedure
Allocation concealment (selection bias)	Low risk	Patients were randomised using the automated randomisation procedure up to 1 week after baseline assessment
ITT analysis	Low risk	For completeness an ITT analysis was performed which rendered very similar results
Blinding of outcome assessment (detection bias) primary outcome	Low risk	Assessors were blinded to group allocation

Manton 2002

Methods	RCT
Participants	Country: USA Sample size: 10 participants Inclusion criteria: 6 months or more post-cerebrovascular accident
Interventions	2 arms: 1. home exercise programme with a mirror exercise unit 2. same programme with a plexiglas exercise unit 1 and 2: 4 weeks
Outcomes	Outcomes were recorded at pre-treatment, mid-treatment, post-treatment and after 3 months • WMFT

Manton 2002 (*Continued)*

Notes	Abstract data only; not included in the analysis due to insufficient data

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Ability matched pairs were created and randomly assigned to groups
Allocation concealment (selection bias)	Unclear risk	Not stated
ITT analysis	Unclear risk	Not stated
Blinding of outcome assessment (detection bias) primary outcome	Unclear risk	Not stated

Michielsen 2011

Methods	RCT
Participants	Country: Netherlands Sample size: 40 participants (20 in each group,; 4 dropped out during intervention period, 4 more dropped out after 6 months) Inclusion criteria: knowledge of Dutch language, Brunnstrom score upper extremity between 3 and 5; home dwelling status; at least 1 year post-stroke Exclusion criteria: neglect; co-morbidities that influenced upper extremity usage; history of multiple strokes
Interventions	2 arms: 1. mirror therapy: participants were instructed to move both arms while looking in the mirror (moving arm covered) 2. bilateral arm training: patients performed the same treatment protocol as in group 1, but without a mirror 1 and 2: once a week physiotherapeutic supervision for 60 minutes; 5 times a week, 60 minutes of practice at home for 6 weeks
Outcomes	Outcomes were recorded at baseline, post-treatment and after 6 months • FM-UE motor score (0 to 66) • Pain (VAS 0 to 100 mm) • Grip force (in kg) • TS elbow and wrist • ARAT (0 to 57) • ABILHAND questionnaire (self-perceived arm use) • Stroke ULAM (accelerometric measurement of arm movements during 24 hours) • EuroQol (quality of life, EQ-5D)

Michielsen 2011 (*Continued)*

Notes	Published and unpublished data

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated random number sequence
Allocation concealment (selection bias)	Low risk	Patients received group allocation after baseline measurement
ITT analysis	Low risk	Results were analysed on an ITT basis
Blinding of outcome assessment (detection bias) primary outcome	Low risk	Assessors were blinded to group allocation

Rothgangel 2004

Methods	RCT; 2 baseline subgroups
Participants	Country: Netherlands Sample size: 16 participants (6 in the outpatient centre group (Rothgangel 2004a), 10 in the inpatient rehabilitation group (Rothgangel 2004b) Inclusion criteria: first stroke in the territory of the middle cerebral artery; minimal 3 months post-stroke; minimal score of 1 in the ARAT Exclusion criteria: bilateral stroke; severe neglect; severe visual impairments
Interventions	2 arms: 1. mirror therapy: patients were instructed to move either both arms (muscle hypotonia), or just the unaffected arm (muscle hypertonia); therapist was moving the affected arm; gross, functional and fine-motor movements were trained 2. bilateral arm training: same treatment protocol as in group 1 but without a mirror 1 and 2: day hospital group (6 participants): 17 treatments during 5 weeks for 30 minutes each; inpatient rehabilitation group (10 participants): 37 treatments during 5 weeks for 30 minutes each
Outcomes	Outcomes were recorded at baseline, in the middle of the treatment, after 5 weeks of treatment and 10 weeks after baseline • ARAT (0 to 57) • Patient-specific problem scale (0 to 100) • Adverse events
Notes	Due to sufficient differences in treatment intensity, we analysed both experimental and both control groups separately Significant differences in baseline characteristics (age, ARAT, patient-specific problem scale)

Rothgangel 2004 (*Continued)*

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer generated random number sequence
Allocation concealment (selection bias)	Low risk	Patients received group allocation after baseline measurement
ITT analysis	Low risk	All patients were analysed as allocated to groups. No drop-outs
Blinding of outcome assessment (detection bias) primary outcome	Low risk	Assessors were blinded to group allocation

Rothgangel 2004a

Methods	RCT; subgroup: outpatient centre
Participants	Country: Netherlands Sample size: 6 participants (3 in each group) Inclusion criteria: first stroke in the territory of the middle cerebral artery; minimal 3 months post-stroke; minimal score of 1 in the ARAT Exclusion criteria: bilateral stroke; severe neglect; severe visual impairments
Interventions	2 arms: 1. mirror therapy: patients were instructed to move either both arms (muscle hypotonia), or just the unaffected arm (muscle hypertonia); therapist was moving the affected arm; gross, functional and fine-motor movements were trained 2. bilateral arm training, same treatment protocol as in group 1 but without a mirror 1 and 2: 17 treatments during 5 weeks for 30 minutes each
Outcomes	Outcomes were recorded at baseline, in the middle of the treatment, after 5 weeks of treatment and 10 weeks after baseline ARAT (0 to 57) Patient-specific problem scale (0 to 100)
Notes	Significant differences in baseline characteristics: patients in the experimental group were younger and had a lower ARAT score

Rothgangel 2004b

Methods	RCT; subgroup: inpatient rehabilitation
Participants	Country: Netherlands Sample size: 10 participants (5 in each group) Inclusion criteria: first stroke in the territory of the middle cerebral artery; minimal 3 months post-stroke; minimal score of 1 in the ARAT Exclusion criteria: bilateral stroke; severe neglect; severe visual impairments
Interventions	2 arms: 1. mirror therapy: patients were instructed to move either both arms (muscle hypotonia), or just the unaffected arm (muscle hypertonia); therapist was moving the affected arm; gross, functional, and fine-motor movements were trained 2. bilateral arm training; same treatment protocol as in group 1 but without a mirror 1 and 2: day hospital group (6 participants): 17 treatments during 5 weeks for 30 minutes each; inpatient rehabilitation group (10 participants): 37 treatments during 5 weeks for 30 minutes each
Outcomes	Outcomes were recorded at baseline, in the middle of the treatment, after 5 weeks of treatment and 10 weeks after baseline ARAT (0 to 57) Patient-specific problem scale (0 to 100)
Notes	Significant differences in baseline characteristics: patients in the experimental group were younger

Seok 2010

Methods	RCT
Participants	Country: South Korea Sample size: 40 participants (19 in mirror therapy group, 21 in control group) Inclusion criteria: stroke within 6 months Exclusion criteria: not able to understand treatment instructions; communication difficulties due to aphasia; MMSE < 15 points; musculoskeletal or neurological damage of the unaffected upperextremity; modified Ashworth Scale of 3 or more points; Brunnstrom stage of recovery (arm) of 1 or more than 5 points
Interventions	2 arms: 1. mirror therapy 2. no additional therapy 1 and 2: 5 days a week, 30 minutes of therapy for 4 weeks
Outcomes	Outcomes were recorded at baseline and after 4 weeks of treatment • MFT • MMT • Grip strength
Notes	Published data only, extracted in part on the basis of an unauthorised, automatic translation of the original publication in Korean Significant difference in MFT between groups at baseline measurement

Seok 2010 *(Continued)*

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer generated random number sequence
Allocation concealment (selection bias)	Unclear risk	Not stated
ITT analysis	Unclear risk	Not stated
Blinding of outcome assessment (detection bias) primary outcome	Low risk	Assessors were blinded to group allocation

Sütbeyaz 2007

Methods	RCT
Participants	Country: Turkey Sample size: 40 participants (20 in each group; 7 dropped out at 6 months follow-up) Inclusion criteria: first unilateral stroke during previous 12 months; a score of 1 or 2 in the Brunnstrom stages of lower extremity; ambulatory before stroke Exclusion criteria: severe cognitive disorders
Interventions	2 arms: 1. mirror therapy: participants were instructed to move the non-paretic leg while looking in the mirror 2. sham therapy: patients performed the same treatment protocol as in group 1 but with the non-reflecting side of the mirror to the non-affected leg 1 and 2: 5 days a week, 30 minutes of therapy for 4 weeks
Outcomes	Outcomes were recorded at baseline, after 4 weeks and after 6 months • Brunnstrom stages lower extremity (0 to 6) • FIM motor items (13 to 91) • MAS (0 to 4)) • FAC (0 to 5)
Notes	

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Block randomisation, computer generated allocation of blocks

Allocation concealment (selection bias)	Low risk	The physicians who assessed potential participants to determine eligibility did not know to which group the participants would be allocated
ITT analysis	High risk	Drop-outs were not included in analysis
Blinding of outcome assessment (detection bias) primary outcome	Low risk	Assessors were blinded to group allocation

Tezuka 2006

Methods	Randomised cross-over trial
Participants	Country: Japan Sample size: 15 participants (9 in mirror therapy group; 6 dropped out, 4 during the first interval) Inclusion criteria: patients admitted or planned to be admitted to rehabilitation ward on the hospital due to post-stroke hemiparesis; within 1 month post-stroke; informed consent was obtained from the patient and their family Exclusion criteria: higher brain dysfunction
Interventions	2 arms: 1. mirror therapy: participants were instructed to move the non-paretic arm while looking in the mirror and passive movement of the paretic arm provided by therapist 2. passive arm movements: using only passive movements of the affected arm without a mirror 1 and 2: 10 to 15 minutes per day for 4 weeks, followed by 4 weeks vice versa
Outcomes	Outcomes were recorded at baseline and after 4 weeks of therapy • FM wrist and fingers motor score (0 to 24)
Notes	We only analysed the first intervention period of 4 weeks

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated allocation to groups
Allocation concealment (selection bias)	High risk	Stated by authors (unpublished information)
ITT analysis	High risk	Stated by authors (unpublished information)
Blinding of outcome assessment (detection bias) primary outcome	Low risk	Assessors were blinded to group allocation

Yavuzer 2008

Methods	RCT
Participants	Country: Turkey Sample size: 40 participants (20 in each group; 4 dropped out at 6 months follow-up) Inclusion criteria: first unilateral stroke during previous 12 months; a Brunnstrom stage between 1 and 4 of the upper extremity; able to understand and follow simple instructions Exclusion criteria: severe cognitive disorders (MMSE < 24)
Interventions	2 arms: 1. mirror therapy: participants were instructed to move both arms while looking in the mirror 2. sham therapy: patients performed the same treatment protocol as in group 1 but with the mirror reflecting the affected arm 1 and 2: 5 days a week, 30 minutes of therapy for 4 weeks
Outcomes	Outcomes were recorded at baseline, after 4 weeks and after 6 months • Brunnstrom stages upper extremity and hand (each 0 to 6) • FIM self-care items (6 to 42) • MAS (0 to 4)
Notes	We combined the Brunnstrom stages of upper extremity and hand into one item using raw data

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomisation, computer generated allocation of blocks
Allocation concealment (selection bias)	Low risk	The physicians who assessed potential participants to determine eligibility did not know to which group the participants would be allocated
ITT analysis	High risk	Drop-outs were not included in the analysis
Blinding of outcome assessment (detection bias) primary outcome	Low risk	Assessors were blinded to group allocation

Yun 2010

Methods	RCT
Participants	Country: South Korea Sample size: 60 participants (20 in each of the 3 groups) Drop-outs during intervention period: 0 Inclusion criteria: first unilateral stroke; Brunnstrom stage I-IV; MMSE > 21

	Exclusion criteria: not stated	
Interventions	3 arms: 1. mirror therapy: patients performed flexion and extension of fingers and wrist while looking in the mirror 2. NMES was applied to extensor muscles on the paretic side and simultaneously underwent flexion and extension of fingers and wrist an the non-paretic side while looking at the wooden board 3. combined mirror therapy and NMES 1,2 and 3: 5 days a week, 30 minutes of therapy for 3 weeks	
Outcomes	Outcomes were recorded at baseline and after 3 weeks of treatment • FM (hand, wrist and co-ordination) • Hand power • Muscle tone	
Notes	Parts of the study were published on the World Stroke Congress 2010 Metaanalysis based on unpublished data We combined group 1 and 3 for analysis using raw data	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random sampling number table as stated by authors (unpublished information)
Allocation concealment (selection bias)	High risk	Stated by authors (unpublished information)
ITT analysis	High risk	Stated by authors (unpublished information)
Blinding of outcome assessment (detection bias) primary outcome	High risk	assessors not blinded, Stated by authors (unpublished information)

ADL: activities of daily living
ARAT: Action Research Arm Test
BI: Barthel Index
CRPS-type 1: complex regional pain syndrome - type I
FAC: Functional Ambulatory Categories
FIM: Functional Independence Measure
FM: Fugl-Meyer Assessment
FM-UE: Fugl-Meyer Assessment upper extremity
ITT: intention-to-treat
MAL: Motor Activity Log
MAS: Motor Assessment Scale
MFT: Manual Function Test

MMSE: Mini Mental State Examination
MMT: Manual Muscle Test
NMES: neuromuscular electrical stimulation
NRS: numeric rating scale
QOM: quality of movement
QST: quantitative sensory testing
RCT: randomised controlled trial
ROM: range of motion
SD: standard deviation
TS: Tardieu Scale
VAS: visual analogue scale
WMFT: Wolf Motor Function Test
WMFT/FA: Wolf Motor Function Test - functional ability
WMFT/PT: Wolf Motor Function Test - performance time

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Adamovich 2009	Study on healthy people
Altschuler 2005	Study on healthy people
Dohle 2009b	Study did not use motor function as primary outcome
Eng 2007	Protocol. Study is not an RCT
Ezendam 2009	Review
Gaggioli 2009	Study is not an RCT
Garry 2005	Study on normal people
Grünert-Plüss 2008	Study is not an RCT
Hamzei 2009	Review
Johnson 1999	Study is not an RCT
Krause 2007	Study was not finished
Merians 2009	Study is not an RCT
Michielsen 2011b	Study is not an RCT
Miltner 1998	Study is not an RCT. Method of randomisation was not adequate
Miltner 1999	Copy of Miltner 1998

(*Continued*)

Miltner 2000	Study is not an RCT
Miltner 2001	Study is not an RCT
Morganti 2003	Protocol. Study is not an RCT
Moseley 2004	Study did not include patients after stroke
Ramachandran 1999	Study is not an RCT
Ramachandran 2009	Review
Rothgangel 2007	Publication of the results of Rothgangel 2004
Sathian 2000	Study is not an RCT
Sathian 2009	Editorial
Shinoura 2008	Study is not an RCT
Stevens 2003	Study is not an RCT
Stevens 2004	Study is not an RCT
Wanschura 2010	Randomised controlled study on healthy people
Zhu 2009	Study is not an RCT. Method of randomisation was not adequate

RCT: randomised controlled trial

Characteristics of studies awaiting assessment *[ordered by study ID]*

Amimoto 2008

Methods	Randomised cross-over trial
Participants	Country: Japan Sample size: 14 participants Inclusion criteria: 4 months and longer after stroke
Interventions	2 arms: 1. mirror therapy for the lower extremity; participants stepped over a columnar step of 3 cm height, 10 times 2. direct condition
Outcomes	• ankle joint angle and time required for the task through a 2-D motion analysis software

Notes	We were not able to include this trial because of unclear outcome of motor function

Characteristics of ongoing studies *[ordered by study ID]*

Dheeraj 2010

Trial name or title	Mirror therapy in unilateral neglect after stoke - MUST
Methods	RCT
Participants	Country: India Inclusion criteria: all stroke patients within 48 hours of onset with thalamic and parietal lobe lesions will be included
Interventions	Setting: stroke unit and College of Physiotherapy 2 arms: 1. mirror therapy with limb activation 2. only limb activation 1 and 2: 20 sessions, 1 to 2 hours each, for 4 weeks
Outcomes	Outcomes will be assessed before treatment, after 4 weeks and 2 months follow-up • Brunnstrom's stage of recovery • star cancellation and line bisection tests • Catherine Bergegoscale • FIM
Starting date	
Contact information	Principal investigator: Dheeraj K, Christian Medical College and Hospital, Physiotherapy, Brown Road, Ludhiana, India Tel: +91 161 2229011 21
Notes	Estimated enrolment: 48 in each group

DRKS00000732

Trial name or title	Mirror therapy as group intervention after stroke: a randomised controlled trial
Methods	RCT
Participants	Country: Germany Inclusion criteria: first supratentorial stroke within the previous 3 months; aged between 18 and 80 years; clinically diagnosed severe hemiparesis or hemiplegia of the distal upper limb with Medical Research Council grading of 0 or 1 of wrist and finger extensors Exclusion criteria: visual impairments that may limit the participation in mirror therapy; severe cognitive and/or language deficits which preclude participants from following instructions in the group training protocol; other neurological or musculoskeletal impairments of the upper extremity not due to stroke; severe neglect

DRKS00000732 (*Continued*)

	(head is not turned to the affected side due to instruction)
Interventions	3 arms: 1. mirror therapy: group intervention; participants exercise in open groups of 2 to 6 patients 2. sham therapy: group intervention; participants exercise in open groups of 2 to 6 patients with the non-reflecting side of the mirror positioned to the unaffected arm 3. mirror therapy, single therapy: participants perform movements with both arms (the affected arm as best as could be) while watching the mirror image of the unaffected arm 1, 2 and 3: 20 sessions, 30 minutes each during 5 weeks
Outcomes	Outcomes will be assessed before and after treatment, and 7 months after treatment • Fugl-Meyer Assessment arm motor score (0 to 66) • Fugl-Meyer Assessment sensory assessment, range of motion and pain arm • ARAT (0 to 57) • Modified Ashworth Scale (0 to 5) • Barthel Index (0 to 100) • Stroke Impact Scale (quality of life) • Neglect: Star Cancellation Test, Line Bisection Test
Starting date	April 2009
Contact information	Principal investigator: Holm Thieme, Schule für Physiotherapie (School for Physiotherapy), Erste Europäische Schule für Physiotherapie, Ergotherapie und Logopädie, Klinik Bavaria Kreischa, Kreischa, Germany Tel: +49 35206 64240 Email: holm.thieme@physiotherapie-schule-kreischa.de
Notes	Estimated enrolment: 66

NCT01010607

Trial name or title	Use of tendon vibration and mirror for the improvement of upper limb function and pain reduction
Methods	RCT
Participants	Country: Israel Inclusion criteria: stroke; 18 to 85 years of age; stroke onset between 1 month and 1 year ago; NIHSS 3 to 15 on study admission; affected upper limb function 10% to 90% on Fugl-Meyer Scale; ability to understand instructions and to move the unaffected limb freely Exclusion criteria: severe cognitive impairment; severe aphasia; severe neglect that impairs ability to understand instructions or to execute tasks
Interventions	3 arms: 1. mirror therapy: moving the healthy hand while watching the mirror 2. tendon vibration and mirror therapy: vibration of 50 Hz to 100 Hz administrated to the elbow and wrist muscles together with the use of a mirror 3. no mirror and sham vibration: moving both hands, the affected hand covered, sham vibration on bones 1, 2 and 3: 10 sessions, 30 minutes each

NCT01010607 *(Continued)*

Outcomes	Outcomes will be assessed after treatment and 3 months after treatment • Fugl Meyer Assessment arm • FIM
Starting date	September 2009
Contact information	Principal Investigator: Elior Moreh, MD, Hadassah University Hospital, Jerusalem, Israel Email: elior@hadassah.org.il
Notes	Estimated enrolment: 30

Thomas 2010

Trial name or title	Mirror arm exercises for stroke
Methods	RCT
Participants	Country: United Kingdom Inclusion criteria: first time stroke at least 1 week previously and inpatient in a stroke rehabilitation unit; no premorbid conditions limiting upper limb function; sufficient cognitive and communication skills to give consent (as judged by the clinical team); medically stable and able to participate in rehabilitation (as judged by the clinical team); upper limb weakness which limits activity (Motricity Index Upper Limb score less than 99) Exclusion criteria: unable to consent; not a first time stroke; previous condition limiting upper limb function; unable to participate in rehabilitation; no upper limb weakness
Interventions	2 arms: 1. mirror therapy for the upper extremity 2. exercises to the legs delivered in the same way as the mirror therapy (but with no mirror) 1 and 2: 30 minutes a day for 4 weeks
Outcomes	Outcomes will be assessed at baseline, immediately after the trial and 1 month after the trial • How well the patient can move and use their weak arm and hand • Acceptability of therapy to patients and clinical team • How much the patients used the treatment • Side effects
Starting date	3 January 2011
Contact information	Principal Investigator: Miss Nessa Thomas, University of Salford, Centre for Rehabilitation and Human Performance Research, Allerton Building, Frederick Road, Salford, UK Email: n.thomas@salford.ac.uk
Notes	Estimated enrolment: 83

ARAT: Action Research Arm Test
FIM: Functional Independence Measure

NIHSS: National Institutes of Health Stroke Scales
RCT: randomised controlled trial

DATA AND ANALYSES

Comparison 1. Mirror therapy versus all other interventions: primary and secondary outcomes

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Motor function at the end of intervention phase	14		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 All studies with post-intervention data	11	481	Std. Mean Difference (IV, Random, 95% CI)	0.61 [0.22, 1.00]
1.2 All studies with change scores	10	283	Std. Mean Difference (IV, Random, 95% CI)	1.04 [0.57, 1.51]
2 Activities of daily living at the end of intervention phase	4		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.1 All studies	4	217	Std. Mean Difference (IV, Fixed, 95% CI)	0.33 [0.05, 0.60]
3 Pain at the end of intervention phase	5		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 All studies	5	188	Std. Mean Difference (IV, Random, 95% CI)	-1.10 [-2.10, -0.09]
4 Visuospatial neglect at the end of intervention	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.1 All studies	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Motor function at follow-up after 6 months	4		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
5.1 All studies	4	157	Std. Mean Difference (IV, Random, 95% CI)	1.09 [0.30, 1.87]

Comparison 2. Subgroup analysis: upper versus lower extremity

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Motor function at the end of intervention	11		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 Mirror therapy for the upper extremity	10	421	Std. Mean Difference (IV, Random, 95% CI)	0.53 [0.04, 1.01]
1.2 Mirror therapy for the lower extremity	1	40	Std. Mean Difference (IV, Random, 95% CI)	0.65 [0.01, 1.29]

Comparison 3. Subgroup analysis: sham intervention (covered mirror) versus other intervention (unrestricted view)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Motor function at the end of intervention phase	9	331	Std. Mean Difference (IV, Random, 95% CI)	0.75 [0.32, 1.19]
1.1 Studies that used a covered mirror in the control group	6	240	Std. Mean Difference (IV, Random, 95% CI)	0.90 [0.27, 1.52]
1.2 Studies that used unrestricted view in the control group	3	91	Std. Mean Difference (IV, Random, 95% CI)	0.42 [0.00, 0.84]

Comparison 4. Sensitivity analysis by trial methodology

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Motor function at the end of intervention	11		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 All studies without randomised cross-over trials	10	466	Std. Mean Difference (IV, Random, 95% CI)	0.59 [0.18, 1.00]
1.2 All studies with a PEDro total score greater than 6 points	7	330	Std. Mean Difference (IV, Random, 95% CI)	0.81 [0.27, 1.36]
1.3 All studies with adequate sequence generation	9	409	Std. Mean Difference (IV, Random, 95% CI)	0.31 [0.09, 0.54]
1.4 All studies with adequate concealed allocation	6	294	Std. Mean Difference (IV, Random, 95% CI)	0.39 [0.12, 0.66]
1.5 All studies with adequate intention-to-treat analysis	5	254	Std. Mean Difference (IV, Random, 95% CI)	0.91 [0.12, 1.71]
1.6 All studies with blinded assessors	10	421	Std. Mean Difference (IV, Random, 95% CI)	0.67 [0.25, 1.10]

Comparison 5. Post-hoc sensitivity analysis removing studies that only included patients with CRPS after stroke

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Motor function at the end of intervention	11		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 All studies	11	481	Std. Mean Difference (IV, Random, 95% CI)	0.61 [0.22, 1.00]
1.2 Without studies that only included patients with CRPS after stroke	9	409	Std. Mean Difference (IV, Random, 95% CI)	0.31 [0.09, 0.54]

2 Pain at the end of intervention phase	5		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 All studies	5	188	Std. Mean Difference (IV, Random, 95% CI)	-1.10 [-2.10, -0.09]
2.2 Without studies that only included patients with CRPS after stroke	3	116	Std. Mean Difference (IV, Random, 95% CI)	-0.16 [-0.53, 0.20]
3 Motor function at follow-up after 6 months	4		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 All studies	4	157	Std. Mean Difference (IV, Random, 95% CI)	1.09 [0.30, 1.87]
3.2 Without studies that only included patients with CRPS after stroke	3	109	Std. Mean Difference (IV, Random, 95% CI)	0.69 [0.26, 1.13]

Analysis 1.1. Comparison 1 Mirror therapy versus all other interventions: primary and secondary outcomes, Outcome 1 Motor function at the end of intervention phase.

Review: Mirror therapy for improving motor function after stroke

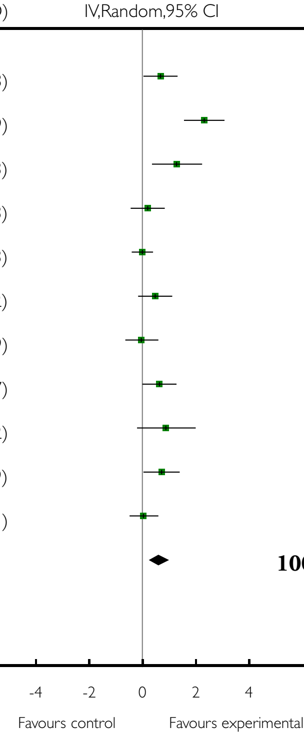
Comparison: 1 Mirror therapy versus all other interventions: primary and secondary outcomes

Outcome: 1 Motor function at the end of intervention phase

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 All studies with post-intervention data							
Acerra 2007	20	3.65 (1.3)	20	2.75 (1.3)		9.4 %	0.68 [0.04, 1.32]
Cacchio 2009a	24	-1.5 (0.7)	24	-3.4 (0.9)		8.6 %	2.32 [1.57, 3.06]
Cacchio 2009b	8	-2.2 (0.7)	16	-3.65 (1.23)		7.3 %	1.28 [0.35, 2.22]
Dohle 2009	18	13.36 (3.16)	18	12.72 (3.33)		9.3 %	0.19 [-0.46, 0.85]
Ietswaart 2011	39	31.51 (20.68)	63	31.61 (20.63)		11.2 %	0.00 [-0.40, 0.39]
Michielsen 2011	20	43.5 (14)	20	36.6 (14.2)		9.5 %	0.48 [-0.15, 1.11]
Seok 2010	19	17.6 (10.5)	21	17.9 (8.9)		9.6 %	-0.03 [-0.65, 0.59]
Sütbeyaz 2007	20	3.5 (0.8)	20	3 (0.7)		9.4 %	0.65 [0.01, 1.29]
Tezuka 2006	9	11.89 (6.23)	6	6.33 (5.2)		6.3 %	0.89 [-0.20, 1.99]
Yavuzer 2008	17	3.62 (1.23)	19	2.79 (0.99)		9.1 %	0.73 [0.05, 1.41]
Yun 2010	40	16.47 (6.83)	20	16.2 (4.1)		10.2 %	0.04 [-0.49, 0.58]
Subtotal (95% CI)	**234**		**247**			**100.0 %**	**0.61 [0.22, 1.00]**

Heterogeneity: Tau² = 0.31; Chi² = 39.46, df = 10 (P = 0.00002); I² =75%

Test for overall effect: Z = 3.07 (P = 0.0022)



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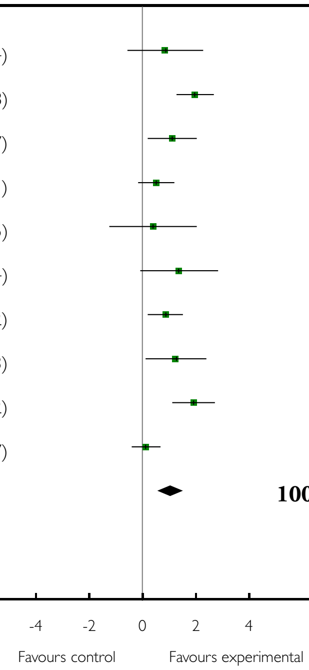
Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
2 All studies with change scores							
Altschuler 1999	4	0.44 (0.24)	5	0.15 (0.34)		6.7 %	0.86 [-0.56, 2.27]
Cacchio 2009a	24	1.5 (0.9)	24	-0.2 (0.8)		12.3 %	1.96 [1.27, 2.66]
Cacchio 2009b	8	1.6 (0.9)	16	0 (1.57)		10.3 %	1.11 [0.19, 2.03]
Dohle 2009	18	9.53 (2.17)	18	8.36 (2.31)		12.6 %	0.51 [-0.15, 1.18]
Rothgangel 2004a	3	5.7 (5)	3	3.6 (3.5)		5.5 %	0.39 [-1.25, 2.03]
Rothgangel 2004b	5	8.4 (5.12)	5	1.2 (4.4)		6.4 %	1.36 [-0.10, 2.82]
Seok 2010	19	5 (5.71)	20	1.26 (1.82)		12.7 %	0.87 [0.21, 1.53]
Tezuka 2006	9	6.44 (3.5)	6	2 (3.03)		8.3 %	1.26 [0.10, 2.41]
Yavuzer 2008	17	0.97 (0.54)	19	0.11 (0.32)		11.3 %	1.92 [1.12, 2.73]
Yun 2010	40	11.55 (6.56)	20	10.8 (3.37)		13.9 %	0.13 [-0.41, 0.67]
Subtotal (95% CI)	**147**		**136**			**100.0 %**	**1.04 [0.57, 1.51]**

Heterogeneity: $Tau^2 = 0.34$; $Chi^2 = 25.51$, df = 9 (P = 0.002); I^2 =65%

Test for overall effect: Z = 4.34 (P = 0.000014)



Analysis 1.2. Comparison 1 Mirror therapy versus all other interventions: primary and secondary outcomes, Outcome 2 Activities of daily living at the end of intervention phase.

Review: Mirror therapy for improving motor function after stroke

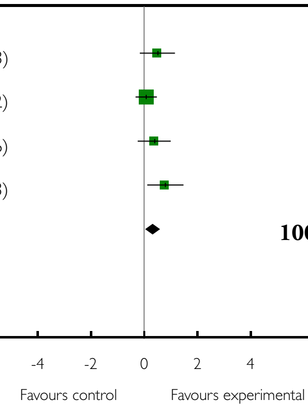
Comparison: 1 Mirror therapy versus all other interventions: primary and secondary outcomes

Outcome: 2 Activities of daily living at the end of intervention phase

Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
1 All studies							
Dohle 2009	18	66.6 (9.4)	18	60.8 (13)		17.0 %	0.50 [-0.16, 1.16]
Ietswaart 2011	39	16.23 (4.13)	66	15.84 (4.72)		47.8 %	0.09 [-0.31, 0.48]
Sütbeyaz 2007	20	65.9 (4.8)	20	61.7 (14.6)		19.1 %	0.38 [-0.25, 1.00]
Yavuzer 2008	17	28.9 (10)	19	22.2 (6.3)		16.1 %	0.79 [0.11, 1.48]
Subtotal (95% CI)	**94**		**123**			**100.0 %**	**0.33 [0.05, 0.60]**

Heterogeneity: $Chi^2 = 3.51$, df = 3 (P = 0.32); I^2 =15%

Test for overall effect: Z = 2.33 (P = 0.020)



Analysis 1.3. Comparison 1 Mirror therapy versus all other interventions: primary and secondary outcomes, Outcome 3 Pain at the end of intervention phase.

Review: Mirror therapy for improving motor function after stroke

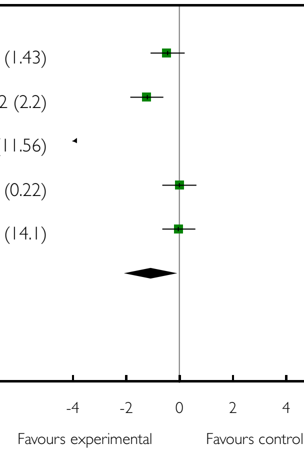
Comparison: 1 Mirror therapy versus all other interventions: primary and secondary outcomes

Outcome: 3 Pain at the end of intervention phase

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Weight	Std. Mean Difference IV,Random,95% CI
1 All studies						
Acerra 2007	20	0.12 (0.34)	20	0.6 (1.43)	22.0 %	-0.45 [-1.08, 0.18]
Cacchio 2009a	24	4.3 (2.5)	24	7.2 (2.2)	22.0 %	-1.21 [-1.83, -0.59]
Cacchio 2009b	8	14.8 (4.5)	16	75.5 (11.56)	12.2 %	-5.93 [-7.96, -3.91]
Dohle 2009	18	1.74 (0.19)	18	1.74 (0.22)	21.8 %	0.0 [-0.65, 0.65]
Michielsen 2011	20	8.8 (10.8)	20	9.2 (14.1)	22.0 %	-0.03 [-0.65, 0.59]
Subtotal (95% CI)	**90**		**98**		**100.0 %**	**-1.10 [-2.10, -0.09]**

Heterogeneity: $Tau^2 = 1.10$; $Chi^2 = 37.08$, df = 4 ($P<0.00001$); $I^2 = 89\%$

Test for overall effect: Z = 2.14 (P = 0.033)



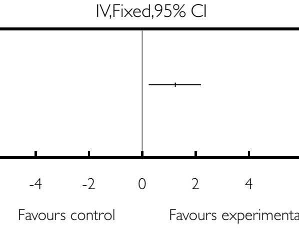
Analysis 1.4. Comparison 1 Mirror therapy versus all other interventions: primary and secondary outcomes, Outcome 4 Visuospatial neglect at the end of intervention.

Review: Mirror therapy for improving motor function after stroke

Comparison: 1 Mirror therapy versus all other interventions: primary and secondary outcomes

Outcome: 4 Visuospatial neglect at the end of intervention

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI
1 All studies					
Dohle 2009	11	-1.36 (0.92)	9	-2.33 (0.5)	1.22 [0.24, 2.19]



Analysis 1.5. Comparison 1 Mirror therapy versus all other interventions: primary and secondary outcomes, Outcome 5 Motor function at follow-up after 6 months.

Review: Mirror therapy for improving motor function after stroke

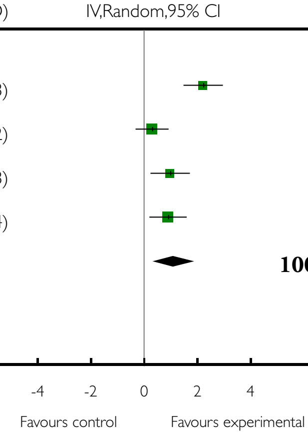
Comparison: 1 Mirror therapy versus all other interventions: primary and secondary outcomes

Outcome: 5 Motor function at follow-up after 6 months

Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 All studies							
Cacchio 2009a	24	-1.9 (1.2)	24	-4.2 (0.8)		24.5 %	2.22 [1.49, 2.95]
Michielsen 2011	20	41.1 (14.9)	20	36.3 (16.2)		26.0 %	0.30 [-0.32, 0.93]
Sütbeyaz 2007	17	4.2 (0.8)	16	3.4 (0.8)		24.5 %	0.98 [0.25, 1.70]
Yavuzer 2008	17	4.18 (1.32)	19	3.05 (1.14)		25.0 %	0.90 [0.21, 1.59]
Subtotal (95% CI)	**78**		**79**			**100.0 %**	**1.09 [0.30, 1.87]**

Heterogeneity: $Tau^2 = 0.52$; $Chi^2 = 15.53$, df = 3 (P = 0.001); $I^2 = 81\%$

Test for overall effect: Z = 2.71 (P = 0.0068)



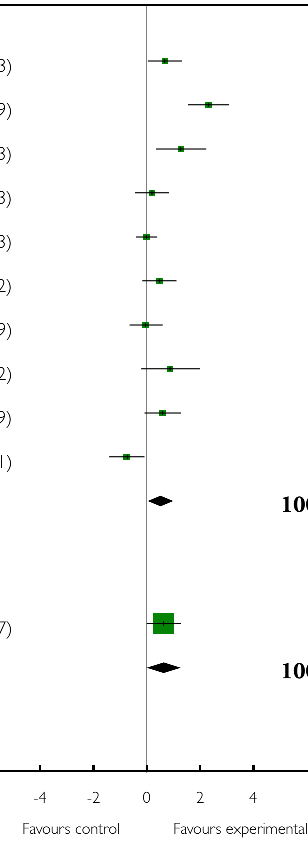
Analysis 2.1. Comparison 2 Subgroup analysis: upper versus lower extremity, Outcome 1 Motor function at the end of intervention.

Review: Mirror therapy for improving motor function after stroke

Comparison: 2 Subgroup analysis: upper versus lower extremity

Outcome: 1 Motor function at the end of intervention

Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Mirror therapy for the upper extremity							
Acerra 2007	20	3.65 (1.3)	20	2.75 (1.3)		10.4 %	0.68 [0.04, 1.32]
Cacchio 2009a	24	-1.5 (0.7)	24	-3.4 (0.9)		9.8 %	2.32 [1.57, 3.06]
Cacchio 2009b	8	-2.2 (0.7)	16	-3.65 (1.23)		8.6 %	1.28 [0.35, 2.22]
Dohle 2009	18	13.36 (3.16)	18	12.72 (3.33)		10.3 %	0.19 [-0.46, 0.85]
Ietswaart 2011	39	31.51 (20.68)	63	31.61 (20.63)		11.7 %	0.00 [-0.40, 0.39]
Michielsen 2011	20	43.5 (14)	20	36.6 (14.2)		10.5 %	0.48 [-0.15, 1.11]
Seok 2010	19	17.6 (10.5)	21	17.9 (8.9)		10.5 %	-0.03 [-0.65, 0.59]
Tezuka 2006	9	11.89 (6.23)	6	6.33 (5.2)		7.7 %	0.89 [-0.20, 1.99]
Yavuzer 2008	17	3.62 (1.23)	19	2.95 (0.99)		10.2 %	0.59 [-0.08, 1.26]
Yun 2010	20	12.35 (5.89)	20	16.2 (4.1)		10.4 %	-0.74 [-1.39, -0.10]
Subtotal (95% CI)	**194**		**227**			**100.0 %**	**0.53 [0.04, 1.01]**
Heterogeneity: Tau^2 = 0.49; Chi^2 = 49.04, df = 9 (P<0.00001); I^2 =82%							
Test for overall effect: Z = 2.12 (P = 0.034)							
2 Mirror therapy for the lower extremity							
Sütbeyaz 2007	20	3.5 (0.8)	20	3 (0.7)		100.0 %	0.65 [0.01, 1.29]
Subtotal (95% CI)	**20**		**20**			**100.0 %**	**0.65 [0.01, 1.29]**
Heterogeneity: not applicable							
Test for overall effect: Z = 2.00 (P = 0.045)							



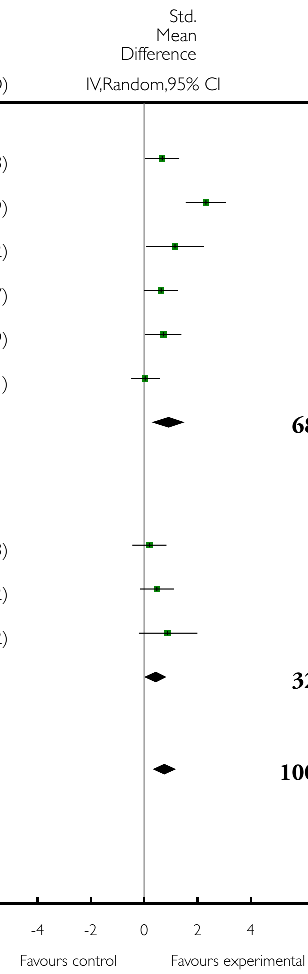
Analysis 3.1. Comparison 3 Subgroup analysis: sham intervention (covered mirror) versus other intervention (unrestricted view), Outcome 1 Motor function at the end of intervention phase.

Review: Mirror therapy for improving motor function after stroke

Comparison: 3 Subgroup analysis: sham intervention (covered mirror) versus other intervention (unrestricted view)

Outcome: 1 Motor function at the end of intervention phase

Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Weight	Std. Mean Difference IV,Random,95% CI
1 Studies that used a covered mirror in the control group						
Acerra 2007	20	3.65 (1.3)	20	2.75 (1.3)	12.0 %	0.68 [0.04, 1.32]
Cacchio 2009a	24	-1.5 (0.7)	24	-3.4 (0.9)	11.0 %	2.32 [1.57, 3.06]
Cacchio 2009b	8	-2.2 (0.7)	8	-3.4 (1.2)	8.1 %	1.15 [0.07, 2.24]
Sütbeyaz 2007	20	3.5 (0.8)	20	3 (0.7)	12.1 %	0.65 [0.01, 1.29]
Yavuzer 2008	17	3.62 (1.23)	19	2.79 (0.99)	11.7 %	0.73 [0.05, 1.41]
Yun 2010	40	16.47 (6.83)	20	16.2 (4.1)	13.0 %	0.04 [-0.49, 0.58]
Subtotal (95% CI)	**129**		**111**		**68.0 %**	**0.90 [0.27, 1.52]**
Heterogeneity: Tau^2 = 0.47; Chi^2 = 24.34, df = 5 (P = 0.00019); I^2 =79%						
Test for overall effect: Z = 2.82 (P = 0.0047)						
2 Studies that used unrestricted view in the control group						
Dohle 2009	18	13.36 (3.16)	18	12.72 (3.33)	11.9 %	0.19 [-0.46, 0.85]
Michielsen 2011	20	43.5 (14)	20	36.6 (14.2)	12.1 %	0.48 [-0.15, 1.11]
Tezuka 2006	9	11.89 (6.23)	6	6.33 (5.2)	8.0 %	0.89 [-0.20, 1.99]
Subtotal (95% CI)	**47**		**44**		**32.0 %**	**0.42 [0.00, 0.84]**
Heterogeneity: Tau^2 = 0.0; Chi^2 = 1.21, df = 2 (P = 0.55); I^2 =0.0%						
Test for overall effect: Z = 1.97 (P = 0.048)						
Total (95% CI)	**176**		**155**		**100.0 %**	**0.75 [0.32, 1.19]**
Heterogeneity: Tau^2 = 0.31; Chi^2 = 27.40, df = 8 (P = 0.00060); I^2 =71%						
Test for overall effect: Z = 3.38 (P = 0.00072)						
Test for subgroup differences: Chi^2 = 1.53, df = 1 (P = 0.22), I^2 =35%						



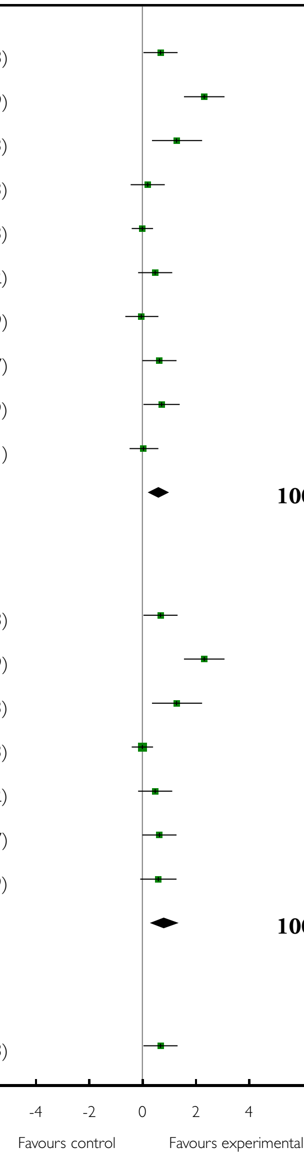
Analysis 4.1. Comparison 4 Sensitivity analysis by trial methodology, Outcome 1 Motor function at the end of intervention.

Review: Mirror therapy for improving motor function after stroke

Comparison: 4 Sensitivity analysis by trial methodology

Outcome: 1 Motor function at the end of intervention

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 All studies without randomised cross-over trials							
Acerra 2007	20	3.65 (1.3)	20	2.75 (1.3)		10.1 %	0.68 [0.04, 1.32]
Cacchio 2009a	24	-1.5 (0.7)	24	-3.4 (0.9)		9.3 %	2.32 [1.57, 3.06]
Cacchio 2009b	8	-2.2 (0.7)	16	-3.65 (1.23)		7.8 %	1.28 [0.35, 2.22]
Dohle 2009	18	13.36 (3.16)	18	12.72 (3.33)		9.9 %	0.19 [-0.46, 0.85]
Ietswaart 2011	39	31.51 (20.68)	63	31.61 (20.63)		11.8 %	0.00 [-0.40, 0.39]
Michielsen 2011	20	43.5 (14)	20	36.6 (14.2)		10.1 %	0.48 [-0.15, 1.11]
Seok 2010	19	17.6 (10.5)	21	17.9 (8.9)		10.2 %	-0.03 [-0.65, 0.59]
Sütbeyaz 2007	20	3.5 (0.8)	20	3 (0.7)		10.1 %	0.65 [0.01, 1.29]
Yavuzer 2008	17	3.62 (1.23)	19	2.79 (0.99)		9.8 %	0.73 [0.05, 1.41]
Yun 2010	40	16.47 (6.83)	20	16.2 (4.1)		10.9 %	0.04 [-0.49, 0.58]
Subtotal (95% CI)	**225**		**241**			**100.0 %**	**0.59 [0.18, 1.00]**
Heterogeneity: Tau² = 0.33; Chi² = 38.85, df = 9 (P = 0.00001); I² =77%							
Test for overall effect: Z = 2.83 (P = 0.0047)							
2 All studies with a PEDro total score greater than 6 points							
Acerra 2007	20	3.65 (1.3)	20	2.75 (1.3)		14.5 %	0.68 [0.04, 1.32]
Cacchio 2009a	24	-1.5 (0.7)	24	-3.4 (0.9)		13.6 %	2.32 [1.57, 3.06]
Cacchio 2009b	8	-2.2 (0.7)	16	-3.65 (1.23)		11.9 %	1.28 [0.35, 2.22]
Ietswaart 2011	39	31.51 (20.68)	63	31.61 (20.63)		16.5 %	0.00 [-0.40, 0.39]
Michielsen 2011	20	43.5 (14)	20	36.6 (14.2)		14.6 %	0.48 [-0.15, 1.11]
Sütbeyaz 2007	20	3.5 (0.8)	20	3 (0.7)		14.6 %	0.65 [0.01, 1.29]
Yavuzer 2008	17	3.62 (1.23)	19	2.95 (0.99)		14.3 %	0.59 [-0.08, 1.26]
Subtotal (95% CI)	**148**		**182**			**100.0 %**	**0.81 [0.27, 1.36]**
Heterogeneity: Tau² = 0.43; Chi² = 31.54, df = 6 (P = 0.00002); I² =81%							
Test for overall effect: Z = 2.91 (P = 0.0037)							
3 All studies with adequate sequence generation							
Acerra 2007	20	3.65 (1.3)	20	2.75 (1.3)		10.3 %	0.68 [0.04, 1.32]



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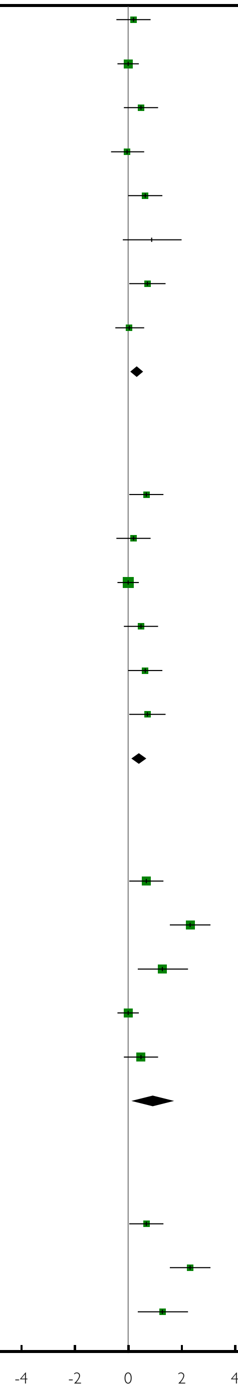
Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Dohle 2009	18	13.36 (3.16)	18	12.72 (3.33)		9.9 %	0.19 [-0.46, 0.85]
Ietswaart 2011	39	31.51 (20.68)	63	31.61 (20.63)		20.9 %	0.00 [-0.40, 0.39]
Michielsen 2011	20	43.5 (14)	20	36.6 (14.2)		10.6 %	0.48 [-0.15, 1.11]
Seok 2010	19	17.6 (10.5)	21	17.9 (8.9)		10.9 %	-0.03 [-0.65, 0.59]
Sütbeyaz 2007	20	3.5 (0.8)	20	3 (0.7)		10.4 %	0.65 [0.01, 1.29]
Tezuka 2006	9	11.89 (6.23)	6	6.33 (5.2)		3.9 %	0.89 [-0.20, 1.99]
Yavuzer 2008	17	3.62 (1.23)	19	2.79 (0.99)		9.4 %	0.73 [0.05, 1.41]
Yun 2010	40	16.47 (6.83)	20	16.2 (4.1)		13.7 %	0.04 [-0.49, 0.58]
Subtotal (95% CI)	**202**		**207**			**100.0 %**	**0.31 [0.09, 0.54]**
Heterogeneity: Tau^2 = 0.02; Chi^2 = 9.80, df = 8 (P = 0.28); I^2 =18%							
Test for overall effect: Z = 2.72 (P = 0.0065)							
4 All studies with adequate concealed allocation							
Acerra 2007	20	3.65 (1.3)	20	2.75 (1.3)		14.6 %	0.68 [0.04, 1.32]
Dohle 2009	18	13.36 (3.16)	18	12.72 (3.33)		14.1 %	0.19 [-0.46, 0.85]
Ietswaart 2011	39	31.51 (20.68)	63	31.61 (20.63)		28.4 %	0.00 [-0.40, 0.39]
Michielsen 2011	20	43.5 (14)	20	36.6 (14.2)		15.0 %	0.48 [-0.15, 1.11]
Sütbeyaz 2007	20	3.5 (0.8)	20	3 (0.7)		14.7 %	0.65 [0.01, 1.29]
Yavuzer 2008	17	3.62 (1.23)	19	2.79 (0.99)		13.3 %	0.73 [0.05, 1.41]
Subtotal (95% CI)	**134**		**160**			**100.0 %**	**0.39 [0.12, 0.66]**
Heterogeneity: Tau^2 = 0.03; Chi^2 = 6.50, df = 5 (P = 0.26); I^2 =23%							
Test for overall effect: Z = 2.79 (P = 0.0053)							
5 All studies with adequate intention-to-treat analysis							
Acerra 2007	20	3.65 (1.3)	20	2.75 (1.3)		20.3 %	0.68 [0.04, 1.32]
Cacchio 2009a	24	-1.5 (0.7)	24	-3.4 (0.9)		19.4 %	2.32 [1.57, 3.06]
Cacchio 2009b	8	-2.2 (0.7)	16	-3.65 (1.23)		17.7 %	1.28 [0.35, 2.22]
Ietswaart 2011	39	31.51 (20.68)	63	31.61 (20.63)		22.1 %	0.00 [-0.40, 0.39]
Michielsen 2011	20	43.5 (14)	20	36.6 (14.2)		20.4 %	0.48 [-0.15, 1.11]
Subtotal (95% CI)	**111**		**143**			**100.0 %**	**0.91 [0.12, 1.71]**
Heterogeneity: Tau^2 = 0.70; Chi^2 = 31.51, df = 4 (P<0.00001); I^2 =87%							
Test for overall effect: Z = 2.25 (P = 0.024)							
6 All studies with blinded assessors							
Acerra 2007	20	3.65 (1.3)	20	2.75 (1.3)		10.5 %	0.68 [0.04, 1.32]
Cacchio 2009a	24	-1.5 (0.7)	24	-3.4 (0.9)		9.7 %	2.32 [1.57, 3.06]
Cacchio 2009b	8	-2.2 (0.7)	16	-3.65 (1.23)		8.2 %	1.28 [0.35, 2.22]



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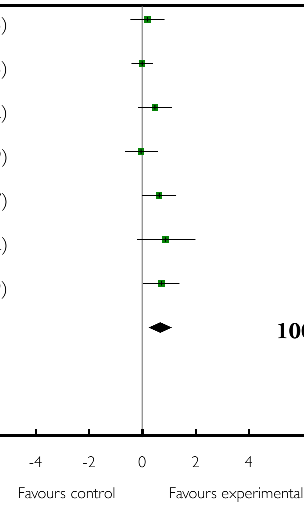
Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Dohle 2009	18	13.36 (3.16)	18	12.72 (3.33)		10.4 %	0.19 [-0.46, 0.85]
Ietswaart 2011	39	31.51 (20.68)	63	31.61 (20.63)		12.3 %	0.00 [-0.40, 0.39]
Michielsen 2011	20	43.5 (14)	20	36.6 (14.2)		10.6 %	0.48 [-0.15, 1.11]
Seok 2010	19	17.6 (10.5)	21	17.9 (8.9)		10.6 %	-0.03 [-0.65, 0.59]
Sütbeyaz 2007	20	3.5 (0.8)	20	3 (0.7)		10.5 %	0.65 [0.01, 1.29]
Tezuka 2006	9	11.89 (6.23)	6	6.33 (5.2)		7.2 %	0.89 [-0.20, 1.99]
Yavuzer 2008	17	3.62 (1.23)	19	2.79 (0.99)		10.2 %	0.73 [0.05, 1.41]
Subtotal (95% CI)	**194**		**227**			**100.0 %**	**0.67 [0.25, 1.10]**

Heterogeneity: Tau^2 = 0.34; Chi^2 = 36.81, df = 9 (P = 0.00003); I^2 =76%

Test for overall effect: Z = 3.12 (P = 0.0018)



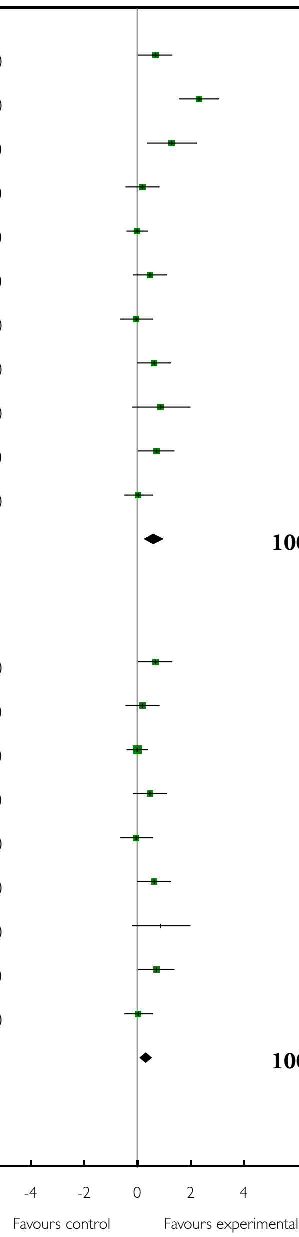
Analysis 5.1. Comparison 5 Post-hoc sensitivity analysis removing studies that only included patients with CRPS after stroke, Outcome 1 Motor function at the end of intervention.

Review: Mirror therapy for improving motor function after stroke

Comparison: 5 Post-hoc sensitivity analysis removing studies that only included patients with CRPS after stroke

Outcome: 1 Motor function at the end of intervention

Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 All studies							
Acerra 2007	20	3.65 (1.3)	20	2.75 (1.3)		9.4 %	0.68 [0.04, 1.32]
Cacchio 2009a	24	-1.5 (0.7)	24	-3.4 (0.9)		8.6 %	2.32 [1.57, 3.06]
Cacchio 2009b	8	-2.2 (0.7)	16	-3.65 (1.23)		7.3 %	1.28 [0.35, 2.22]
Dohle 2009	18	13.36 (3.16)	18	12.72 (3.33)		9.3 %	0.19 [-0.46, 0.85]
Ietswaart 2011	39	31.51 (20.68)	63	31.61 (20.63)		11.2 %	0.00 [-0.40, 0.39]
Michielsen 2011	20	43.5 (14)	20	36.6 (14.2)		9.5 %	0.48 [-0.15, 1.11]
Seok 2010	19	17.6 (10.5)	21	17.9 (8.9)		9.6 %	-0.03 [-0.65, 0.59]
Sütbeyaz 2007	20	3.5 (0.8)	20	3 (0.7)		9.4 %	0.65 [0.01, 1.29]
Tezuka 2006	9	11.89 (6.23)	6	6.33 (5.2)		6.3 %	0.89 [-0.20, 1.99]
Yavuzer 2008	17	3.62 (1.23)	19	2.79 (0.99)		9.1 %	0.73 [0.05, 1.41]
Yun 2010	40	16.47 (6.83)	20	16.2 (4.1)		10.2 %	0.04 [-0.49, 0.58]
Subtotal (95% CI)	**234**		**247**			**100.0 %**	**0.61 [0.22, 1.00]**
Heterogeneity: Tau^2 = 0.31; Chi^2 = 39.46, df = 10 (P = 0.00002); I^2 =75%							
Test for overall effect: Z = 3.07 (P = 0.0022)							
2 Without studies that only included patients with CRPS after stroke							
Acerra 2007	20	3.65 (1.3)	20	2.75 (1.3)		10.3 %	0.68 [0.04, 1.32]
Dohle 2009	18	13.36 (3.16)	18	12.72 (3.33)		9.9 %	0.19 [-0.46, 0.85]
Ietswaart 2011	39	31.51 (20.68)	63	31.61 (20.63)		20.9 %	0.00 [-0.40, 0.39]
Michielsen 2011	20	43.5 (14)	20	36.6 (14.2)		10.6 %	0.48 [-0.15, 1.11]
Seok 2010	19	17.6 (10.5)	21	17.9 (8.9)		10.9 %	-0.03 [-0.65, 0.59]
Sütbeyaz 2007	20	3.5 (0.8)	20	3 (0.7)		10.4 %	0.65 [0.01, 1.29]
Tezuka 2006	9	11.89 (6.23)	6	6.33 (5.2)		3.9 %	0.89 [-0.20, 1.99]
Yavuzer 2008	17	3.62 (1.23)	19	2.79 (0.99)		9.4 %	0.73 [0.05, 1.41]
Yun 2010	40	16.47 (6.83)	20	16.2 (4.1)		13.7 %	0.04 [-0.49, 0.58]
Subtotal (95% CI)	**202**		**207**			**100.0 %**	**0.31 [0.09, 0.54]**
Heterogeneity: Tau^2 = 0.02; Chi^2 = 9.80, df = 8 (P = 0.28); I^2 =18%							
Test for overall effect: Z = 2.72 (P = 0.0065)							



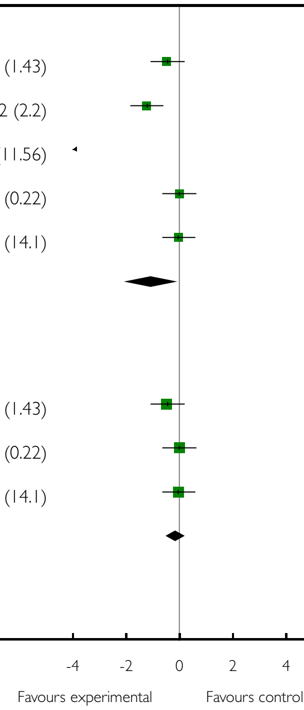
Analysis 5.2. Comparison 5 Post-hoc sensitivity analysis removing studies that only included patients with CRPS after stroke, Outcome 2 Pain at the end of intervention phase.

Review: Mirror therapy for improving motor function after stroke

Comparison: 5 Post-hoc sensitivity analysis removing studies that only included patients with CRPS after stroke

Outcome: 2 Pain at the end of intervention phase

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 All studies							
Acerra 2007	20	0.12 (0.34)	20	0.6 (1.43)		22.0 %	-0.45 [-1.08, 0.18]
Cacchio 2009a	24	4.3 (2.5)	24	7.2 (2.2)		22.0 %	-1.21 [-1.83, -0.59]
Cacchio 2009b	8	14.8 (4.5)	16	75.5 (11.56)		12.2 %	-5.93 [-7.96, -3.91]
Dohle 2009	18	1.74 (0.19)	18	1.74 (0.22)		21.8 %	0.0 [-0.65, 0.65]
Michielsen 2011	20	8.8 (10.8)	20	9.2 (14.1)		22.0 %	-0.03 [-0.65, 0.59]
Subtotal (95% CI)	**90**		**98**			**100.0 %**	**-1.10 [-2.10, -0.09]**
Heterogeneity: $Tau^2 = 1.10$; $Chi^2 = 37.08$, df = 4 (P<0.00001); I^2 =89%							
Test for overall effect: Z = 2.14 (P = 0.033)							
2 Without studies that only included patients with CRPS after stroke							
Acerra 2007	20	0.12 (0.34)	20	0.6 (1.43)		33.9 %	-0.45 [-1.08, 0.18]
Dohle 2009	18	1.74 (0.19)	18	1.74 (0.22)		31.3 %	0.0 [-0.65, 0.65]
Michielsen 2011	20	8.8 (10.8)	20	9.2 (14.1)		34.8 %	-0.03 [-0.65, 0.59]
Subtotal (95% CI)	**58**		**58**			**100.0 %**	**-0.16 [-0.53, 0.20]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.23$, df = 2 (P = 0.54); I^2 =0.0%							
Test for overall effect: Z = 0.88 (P = 0.38)							



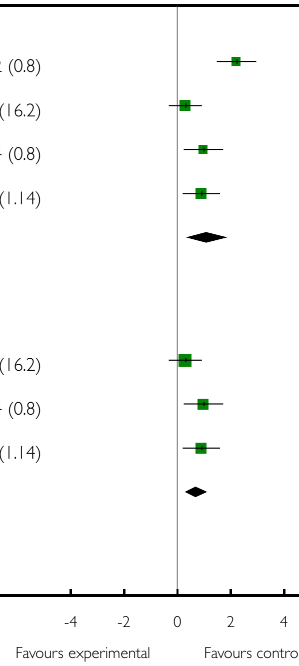
Analysis 5.3. Comparison 5 Post-hoc sensitivity analysis removing studies that only included patients with CRPS after stroke, Outcome 3 Motor function at follow-up after 6 months.

Review: Mirror therapy for improving motor function after stroke

Comparison: 5 Post-hoc sensitivity analysis removing studies that only included patients with CRPS after stroke

Outcome: 3 Motor function at follow-up after 6 months

Study or subgroup	Experimental N	Experimental Mean(SD)	Control N	Control Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 All studies							
Cacchio 2009a	24	-1.9 (1.2)	24	-4.2 (0.8)		24.5 %	2.22 [1.49, 2.95]
Michielsen 2011	20	41.1 (14.9)	20	36.3 (16.2)		26.0 %	0.30 [-0.32, 0.93]
Sütbeyaz 2007	17	4.2 (0.8)	16	3.4 (0.8)		24.5 %	0.98 [0.25, 1.70]
Yavuzer 2008	17	4.18 (1.32)	19	3.05 (1.14)		25.0 %	0.90 [0.21, 1.59]
Subtotal (95% CI)	**78**		**79**			**100.0 %**	**1.09 [0.30, 1.87]**
Heterogeneity: Tau^2 = 0.52; Chi^2 = 15.53, df = 3 (P = 0.001); I^2 =81%							
Test for overall effect: Z = 2.71 (P = 0.0068)							
2 Without studies that only included patients with CRPS after stroke							
Michielsen 2011	20	41.1 (14.9)	20	36.3 (16.2)		38.1 %	0.30 [-0.32, 0.93]
Sütbeyaz 2007	17	4.2 (0.8)	16	3.4 (0.8)		29.6 %	0.98 [0.25, 1.70]
Yavuzer 2008	17	4.18 (1.32)	19	3.05 (1.14)		32.3 %	0.90 [0.21, 1.59]
Subtotal (95% CI)	**54**		**55**			**100.0 %**	**0.69 [0.26, 1.13]**
Heterogeneity: Tau^2 = 0.03; Chi^2 = 2.43, df = 2 (P = 0.30); I^2 =18%							
Test for overall effect: Z = 3.16 (P = 0.0016)							



ADDITIONAL TABLES

Table 1. Patient characteristics of included studies

Study ID	Experimental: age, mean (SD)	Control: age, mean (SD)	Experimental: time post-stroke	Control: time post-stroke	Experimental: sex	Control: sex	Experimental: side paresis	Control: side paresis
Acerra 2007	65.9 (11.5) years	70.8 (5.4) years	5.2 (3.4) days	5.4 (2.7) days	12 female, 8 male	10 female, 10 male	8 left, 12 right	8 left, 12 right
Altschuler 1999	55.8 (4.3) years	60.2 (7.6) years	1.85 (1.98) years	7.72 (10.48) years	2 female, 2 male	2 female, 3 male	1 left, 3 right	0 left, 5 right

Table 1. Patient characteristics of included studies *(Continued)*

Cacchio 2009a	57.9 (9.9) years	58.8 (9.4) years	5.1 (2.5) months	4.9 (2.8) months	13 female, 11 male	13 female, 11 male	16 left, 8 right	18 left, 6 right
Cacchio 2009b	63.4 (9.7) years	Control 1: 61.8 (8.4) years Control 2: 62.3 (9.2) years	16.8 (6.6) months	Control 1: 14.9 (4.8) months Control 2: 15.4 (5.3) months	4 female, 4 male	Control 1: 5 female, 3 male Control 2: 4 female, 4 male	5 left, 3 right	Control 1: 5 left, 3 right Control 2: 5 left, 3 right
Dohle 2009	54.9 (13.8) years	58.0 (14.0) years	26.2 (8.3) days	27.8 (12.1) days	5 female, 13 male	5 female, 13 male	Not provided	Not provided
Ietswaart 2011	69.3 (10.8) years	Control 1: 68.6 (16.3) years Control 2: 64.4 (15.9) years	82.0 (55.0) days	Control 1: 90.8 (63.4) days Control 2: 80.5 (62.7) days	18 female, 23 male	Control 1: 17 female, 22 male Control 2: 16 female, 25 male	24 left, 17 right	Control 1: 23 left, 16 right Control 2: 22 left, 19 right
Manton 2002	Not provided	Not provided	Not provided	Not provided	Not provided	Not provided	Not provided	Not provided
Michielsen 2011	55.3 (12.0) years	58.7 (13.5) years	4.7 (3.6) years	4.5 (2.6) years	13 female, 7 male	7 female, 13 male	6 dominant, 14 non-dominant	6 dominant, 14 non-dominant
Rothgangel 2004	Experimental 1: 74.0 (12.5) years Experimental 2: 72.0 (15.3) years	Control 1: 77.7 (4.9) years Control 2: 72.0 (15.3) years	Median (range) Experimental 1: 12 (9 to 15) months Experimental 2: 7 (3 to 14) months	Median (range) Control 1: 12 (5 to 18) months Control 2: 7 (5 to 24) months	6 female, 2 male	4 female, 4 male	Experimental 1: 2 left, 1 right Experimental 2: 3 left, 2 right	Control 1: 1 left, 2 right Control 2: 2 left, 3 right
Seok 2010	56.4 (14.8) years	46.4 (21.5) years	4.3 (1.6) months	3.7 (1.9) months	8 female, 11 male	10 female, 11 male	11 left, 8 right	6 left, 14 right
Sütbeyaz 2007	62.7 (9.7) years	64.7 (7.7) years	3.5 (1.3) months	3.9 (1.9) months	10 female, 10 male	7 female, 13 male	14 left, 6 right	13 left, 7 right
Tezuka 2006	64.6 (16.5) years	63.7 (10.3) years	38.3 (16.5) days	29.7 (8.2) days	4 female, 5 male	5 female, 1 male	4 left, 5 right	2 left, 4 right
Yavuzer 2008	63.2 (9.2) years	63.3 (9.5) years	5.4 (2.9) months	5.5 (2.5) months	8 female, 9 male	9 female, 10 male	10 left, 7 right	11 left, 8 right

Table 1. Patient characteristics of included studies *(Continued)*

Yun 2010	63.1 (7.8) years	61.4 (8.7) years	3.4 (1.6) weeks	4.1 (1.8) weeks	14 female, 6 male	13 female, 7 male	11 left, 9 right	12 left, 8 right

SD: standard deviation

Table 2. Characteristics of interventions of included studies

Study ID	Extremity	Mirror therapy variation	Control intervention	Type of movements	Minutes per session	Sessions per week	Total duration (weeks)	Total amount of therapy (minutes)	Setting
Acerra 2007	Upper extremity	Bilateral activities	Bilateral activities; covered mirror	Functional motor tasks (i. e. with objects); motor coordination tasks; sensory discrimination tasks; grip strength; active range of motion	20 to 30	7	14	280 to 420	Inpatient hospital
Altschuler 1999	Upper extremity	Bilateral activities	Bilateral activities; transparent plastic between limbs	Proximal and distal movements	15, 2 times a day	12	4 (first period)	720	Not stated
Cacchio 2009a	Upper extremity	Activities of the unaffected limb	Activities of the unaffected limb; covered mirror	Flexion/ extension of shoulder, elbow and wrist; prone/ supination forearm	30 first 2 weeks; 60 last 2 weeks	5	4	900	Inpatient and outpatient rehabilitation centre

Table 2. Characteristics of interventions of included studies *(Continued)*

Cacchio 2009b	Upper extremity	Activities of the unaffected limb	Activities of the unaffected limb; covered mirror (control group 1); imagination of movements of the affected limb (control group 2)	Flexion/ extension of shoulder, elbow and wrist; prone/ supination forearm	30	Daily	4	840	Inpatient and outpatient rehabilitation centre
Dohle 2009	Upper extremity	Bilateral activities	Bilateral activities; without mirror	Execution of arm, hand and finger postures	30	5	6	900	Inpatient rehabilitation centre
Ietswaart 2011	Upper extremity	Activities of the unaffected limb (additionally to a motor imagery intervention)	Control 1: mental rehearsal of non-motor related images Control 2: standard care	Elementary movements and patient selected movements	10	1 to 2	4	60	Hospital and home
Manton 2002	Upper extremity	Not stated	Not stated; transparent plastic between limbs	Not stated	Not stated	Not stated	4	Not stated	Home
Michielsen 2011	Upper extremity	Bilateral activities; once a week under supervision; 5 times a week at home	Bilateral activities; once a week under supervision, 5 times a week at home;	Exercises based on the Brunnstrom phases of motor recovery; functional tasks (i.	60	1 (under supervision) + 5 (at home)	6	2160	Home

Table 2. Characteristics of interventions of included studies *(Continued)*

			without mirror	e. with objects)					
Rothgangel 2004a	Upper extremity	Bilateral activities (hypotone muscles); unilateral activities (hypertone muscles)	Bilateral activities; without mirror	Gross motor arm and hand movements; functional activities (i. e. with objects); fine motor activities (i. e. with objects)	30	Total number of sessions: 17	5	510	Outpatient centre
Rothgangel 2004b	Upper extremity	Bilateral activities (hypotone muscles); unilateral activities (hypertone muscles)	Bilateral activities; without mirror	Gross motor arm and hand movements; functional activities (i. e. with objects); fine motor activities (i. e. with objects)	30	Total number of sessions: 37	5	1110	Inpatient rehabilitation centre
Seok 2010	Upper extremity	Activities of the unaffected limb	No therapy	5 movements of wrist and fingers, each 6 minutes	30	5	4	500	Inpatient rehabilitation centre
Sütbeyaz 2007	Lower extremity	Activities of the unaffected limb	Activities of the unaffected limb; covered mirror	Dorsiflexion movements of the ankle	30	5	4	600	Inpatient rehabilitation centre
Tezuka 2006	Upper extremity	Activities of the	Activities of the	13 kinds of move-	10 to 15	Daily	4 (first period)	280 to 420	Inpatient rehabilita-

		unaffected limb; affected limb passively moved by therapist	unaffected limb; affected limb passively moved by therapist; without mirror	ments, i.e. flexion/extension of wrist, pinching fingers, gripping ball						tion centre
Yavuzer 2008	Upper extremity	Activities of the unaffected limb	Activities of the unaffected limb; covered mirror	Flexion/ extension of wrist and fingers	30	5	4	600	Inpatient rehabilitation centre
Yun 2010	Upper extremity	Experimental 1: activities of the unaffected limb Experimental 2: activities of the unaffected limb and additionally neuromuscular electrical stimulation of the affected arm	Neuromuscular electrical stimulation of finger and wrist extensors of the affected arm	Flexion/ extension of wrist and fingers	30	5	3	450	Inpatient rehabilitation centre

Table 3. PEDro score of included studies

	Acerra 2007	Altschuler 1999	Cacchio 2009a	Cacchio 2009b	Dohle 2009	Ietswaart 2011	Manton 2002	Michielsen 2011	Rothgangel 2004	Seok 2010	Sütbeyaz 2007	Tezuka 2006	Yavuzer 2008	Yun 2010
Random allocation	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Concealed allo-	Yes	Unclear	Unclear	Yes	Yes	Yes	Unclear	Yes	Yes	Unclear	Yes	No	Yes	No

Table 3. PEDro score of included studies *(Continued)*

cation														
Baseline comparability	Yes	No	Yes	Yes	Yes	Yes	Unclear	Yes	No	No	Yes	Yes	Yes	Yes
Blind participants	No	No	No	No	No	No	Unclear	No	No	No	No	No	No	No
Blind therapists	No	No	No	No	No	No	Unclear	No	No	No	No	No	No	No
Blind assessors	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	No
Adequate follow-up	Yes	No	Yes	Yes	No	Yes	Unclear	Yes	Yes	Unclear	Yes	No	Yes	Yes
Intention-to-treat	Yes	No	Yes	Yes	No	Yes	Unclear	Yes	Yes	Unclear	No	No	No	No
Between group comparisons	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Point estimates and variability	Yes	No	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Total PE-	8/10	3/10	7/10	8/10	6/10	8/10	1/10	8/10	7/10	4/10	7/10	5/10	7/10	5/10

Table 3. PEDro score of included studies *(Continued)*

Dro score														

APPENDICES

Appendix 1. MEDLINE search strategy

MEDLINE (Ovid) 1950 to June 2011

1. cerebrovascular disorders/ or exp basal ganglia cerebrovascular disease/ or exp brain ischemia/ or exp carotid artery diseases/ or exp intracranial arterial diseases/ or exp intracranial arteriovenous malformations/ or exp "intracranial embolism and thrombosis"/ or exp intracranial hemorrhages/ or stroke/ or exp brain infarction/
2. brain injuries/ or brain injury, chronic/
3. (stroke$ or cva or poststroke or post-stroke).tw.
4. (cerebrovasc$ or cerebral vascular).tw.
5. (cerebral or cerebellar or brain$ or vertebrobasilar).tw.
6. (infarct$ or isch?emi$ or thrombo$ or emboli$ or apoplexy).tw.
7. 5 and 6
8. (cerebral or brain or subarachnoid).tw.
9. (haemorrhage or hemorrhage or haematoma or hematoma or bleed$).tw.
10. 8 and 9
11. exp hemiplegia/ or exp paresis/
12. (hempar$ or paretic or paresis or hemipleg$ or brain injur$).tw.
13. Gait Disorders, Neurologic/
14. 1 or 2 or 3 or 4 or 7 or 10 or 11 or 12 or 13
15. exp Upper Extremity/
16. (upper limb$ or upper extremit$ or arm or shoulder or hand or axilla or elbow$ or forearm$ or finger$ or wrist$).tw.
17. exp Lower Extremity/
18. (lower limb$ or lower extremit$ or buttock$ or foot or feet or hip or hips or knee or knees or leg or legs or thigh$ or ankle$ or heel$ or toe or toes).tw.
19. 15 or 16 or 17 or 18
20. Illusions/
21. (mirror$ or visual$ or virtual$).tw.
22. (visual adj5 (reflection or illusion or feedback or therapy)).tw.
23. ((limb$ or arm or leg) adj5 (reflect or reflection or illusion)).tw.
24. 20 or 21 or 22 or 23
25. 14 and 19 and 24

Appendix 2. EMBASE search strategy

1 exp basal ganglia cerebrovascular disease/
2 cerebrovascular disorders/
3 exp intracranial arterial diseases/
4 exp intracranial arteriovenous malformations/
5 exp "intracranial embolism and thrombosis"/
6 exp intracranial hemorrhages/
7 stroke/
8 exp brain infarction/
9 exp brain ischemia/
10 exp carotid artery diseases/
11 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12 (brain injuries or brain injury, chronic).af.
13 (stroke$ or cva or poststroke or post-stroke tw).af.
14 (cerebrovasc$ or cerebral vascular tw).af.
15 (cerebral or cerebellar or brain$ or vertebrobasilar tw).af.
16 (infarct$ or ish?emi$ or thrombo$ or emboli$ or apoplexy tw).af.
17 15 and 16
18 (cerebral or brain or subarachnoid tw).af.
19 (haemorrhage or hemorrhage or haematoma or hematoma or bleed$ tw).af.
20 18 and 19
21 exp hemiplegia/ or exp paresis/
22 (hempar$ or paretic or paresis or hemipleg$ or brain injur$).tw.
23 Gait Disorders, Neurologic/
24 11 or 12 or 13 or 14 or 17 or 20 or 21 or 22 or 23
25 exp Upper Extremity/
26 (upper limb$ or upper extremit$ or arm or shoulder or hand or axilla or elbow$ or forearm$ or finger$ or wrist$).tw.
27 exp Lower Extremity/
28 (lower lib$ or lower extremit$ or buttock$ or foot or feet or hip or hips or knee or knees or leg or legs or thigh$ or ankle$ or heel$ or toe or toes).tw.
29 25 or 26 or 27 or 28
30 Illusions/
31 mirror$.tw.
32 (visual adj5 (refelction or illusion or feedback or therapy)).tw.
33 ((limb$ or arm or leg) adj5 (reflect or reflection or illusion)).tw.
34 30 or 31 or 32 or 33
35 24 and 29 and 34 (309)

Appendix 3. CINAHL search strategy

CINAHL (Ebsco) 1982 to June 2011

1. (MH "Cerebrovascular Disorders+") or (MH "stroke patients") or (MH "stroke units")
2. TI (stroke or poststroke or post-stroke or cerebrovasc* or cerebral vasc or cva) or AB (stroke or poststroke or post-stroke or cerebrovasc* or cerebral vasc or cva)
3. TI (brain* or cerebr* or cerebell* or vertebrobasilar) or AB (brain* or cerebr* or cerebell* or vertebrobasilar)
4. TI (ischemi* or ischaemi* or infarct* or thrombo* or emboli* or apoplexy*) or AB (ischemi* or ischaemi* or infarct* or thrombo* or emboli* or apoplexy*)
5. 3 and 4
6. TI (brain* or cerebr* or cerebell* or subarachnoid) or AB (brain* or cerebr* or cerebell* or subarachnoid)
7. TI (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*) or AB (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*)
8. 6 and 7

9. (MH “Hemiplegia”)
10. TI (hemipleg* or hemipar* or paresis or paretic or brain injur*) or AB (hemipleg* or hemipar* or paresis or paretic or brain injur*)
11. (MH “Brain Injuries”)
12. 1 or 2 or 5 or 8 or 9 or 10 or 11
13. (MH “Upper Extremity+”)
14. TI (upper limb* or upper extremit* or arm or shoulder or hand or axilla or elbow* or forearm* or finger* or wrist*) or AB (upper limb* or upper extremit* or arm or shoulder or hand or axilla or elbow* or forearm* or finger* or wrist*)
15. (MH “Lower Extremity+”)
16. TI (lower limb* or lower extremit* or buttock* or foot or feet or hip or hips or knee or knees or leg or legs or thigh* or ankle* or heel* or toe or toes) or AB (lower limb* or lower extremit* or buttock* or foot or feet or hip or hips or knee or knees or leg or legs or thigh* or ankle* or heel* or toe or toes)
17. 13 or 14 or 15 or 16
18. (MH “Illusions+”)
19. (MH “Reflection”)
20. TI (mirror* or video* or virtual*) and AB (mirror* or video* or virtual*)
21. TI (reflect or reflection or illusion or visual feedback) or AB (reflect or reflection or illusion or visual feedback)
22. 18 or 19 or 20 or 21
23. 12 and 17 and 22

CONTRIBUTIONS OF AUTHORS

Holm Thieme (HT) and Christian Dohle (CD) were involved in all stages of the review and contributed to the conception and design of the review. Jan Mehrholz (JM) was involved in methodological planning and conducting the review, statistical analysis of outcome data and interpreting the results. Johann Behrens (JB) and Marcus Pohl (MP) were involved in extracting data, assessing the methodological quality of selected studies and interpreting the results. All authors approved the protocol and the final review.

DECLARATIONS OF INTEREST

Holm Thieme (HT) is principal investigator of an ongoing trial that may be relevant for the topic of this review. He has received and will receive honorarium for presentations and seminars on mirror therapy.

Christian Dohle (CD) is first author of one of the included studies on the effect of mirror therapy after stroke. He was not involved in checking this trial for eligibility, extracting data and assessing the methodological quality of the study. He has received and will receive honorarium for presentations and seminars on mirror therapy and is co-author of a corresponding therapy manual (Nakaten 2009).

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Internal sources

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External sources

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We added a further database for searching ongoing studies: International Clinical Trials Registry Platform (ICTRP).

We previously planed to perform a subgroup analysis comparing studies that included participants with different severities of motor impairment. Based on the baseline data for motor function we were not able to clearly differentiate studies based on this criteria, except in one study that only included participants with severe motor impairment (Dohle 2009). The other studies included participants with mixed severities of motor impairments. Due to these problems of differentiation, we decided not to do this subgroup analysis.

Two studies (Cacchio 2009a; Cacchio 2009b) only included patients after stroke with a diagnosis of CRPS-type I, which might have influenced the effects of the intervention. Thus, we performed a post-hoc sensitivity analysis by removing these studies; that was not planned in the protocol.

INDEX TERMS

Medical Subject Headings (MeSH)

*Recovery of Function; *Stroke Rehabilitation; Activities of Daily Living; Exercise Movement Techniques [instrumentation; *methods]; Functional Laterality [physiology]; Paresis [etiology; *rehabilitation]; Randomized Controlled Trials as Topic; Stroke [complications]

MeSH check words

Humans